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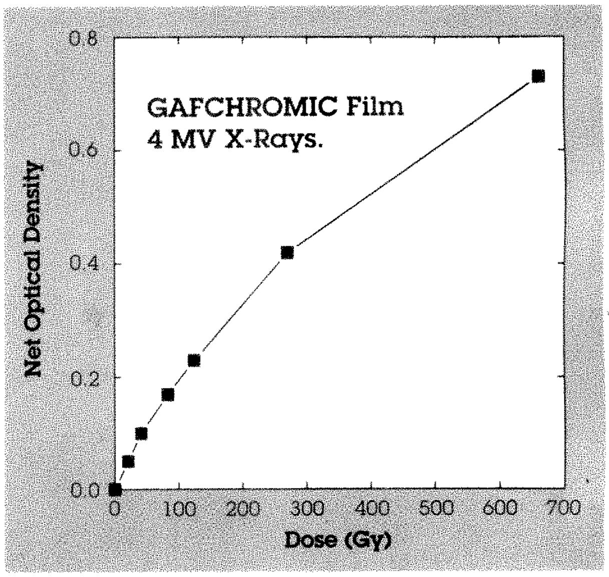

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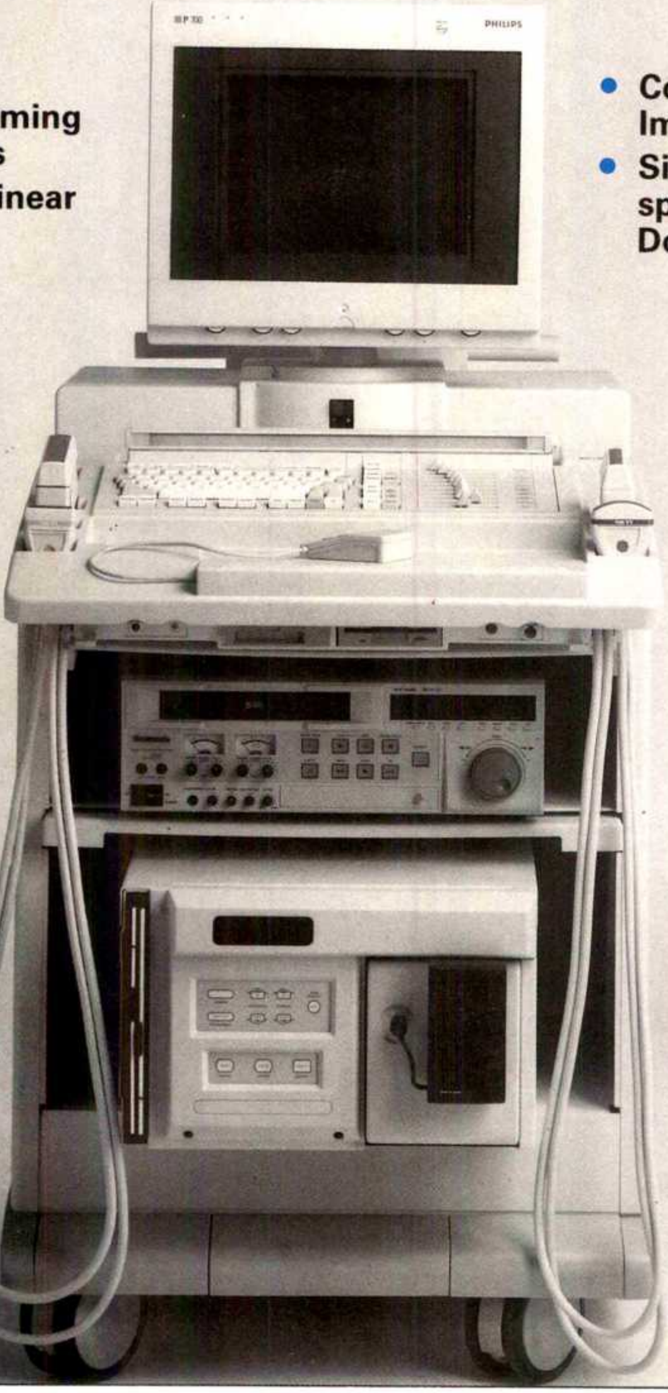

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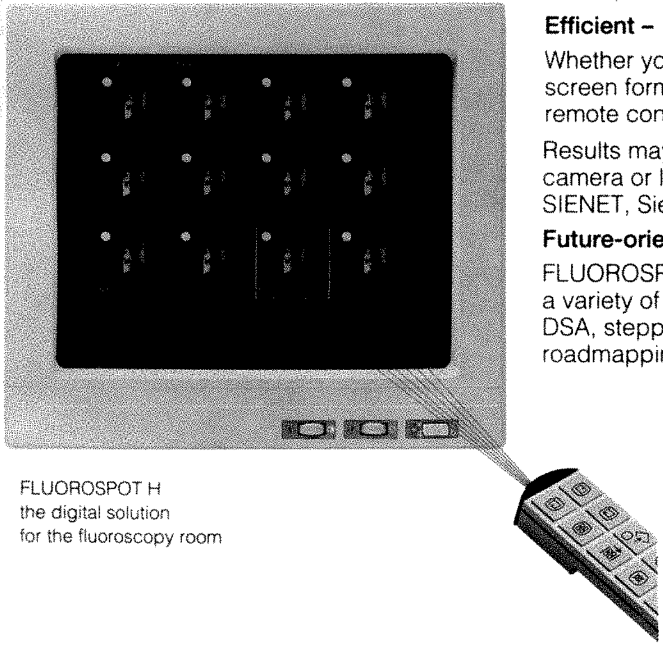

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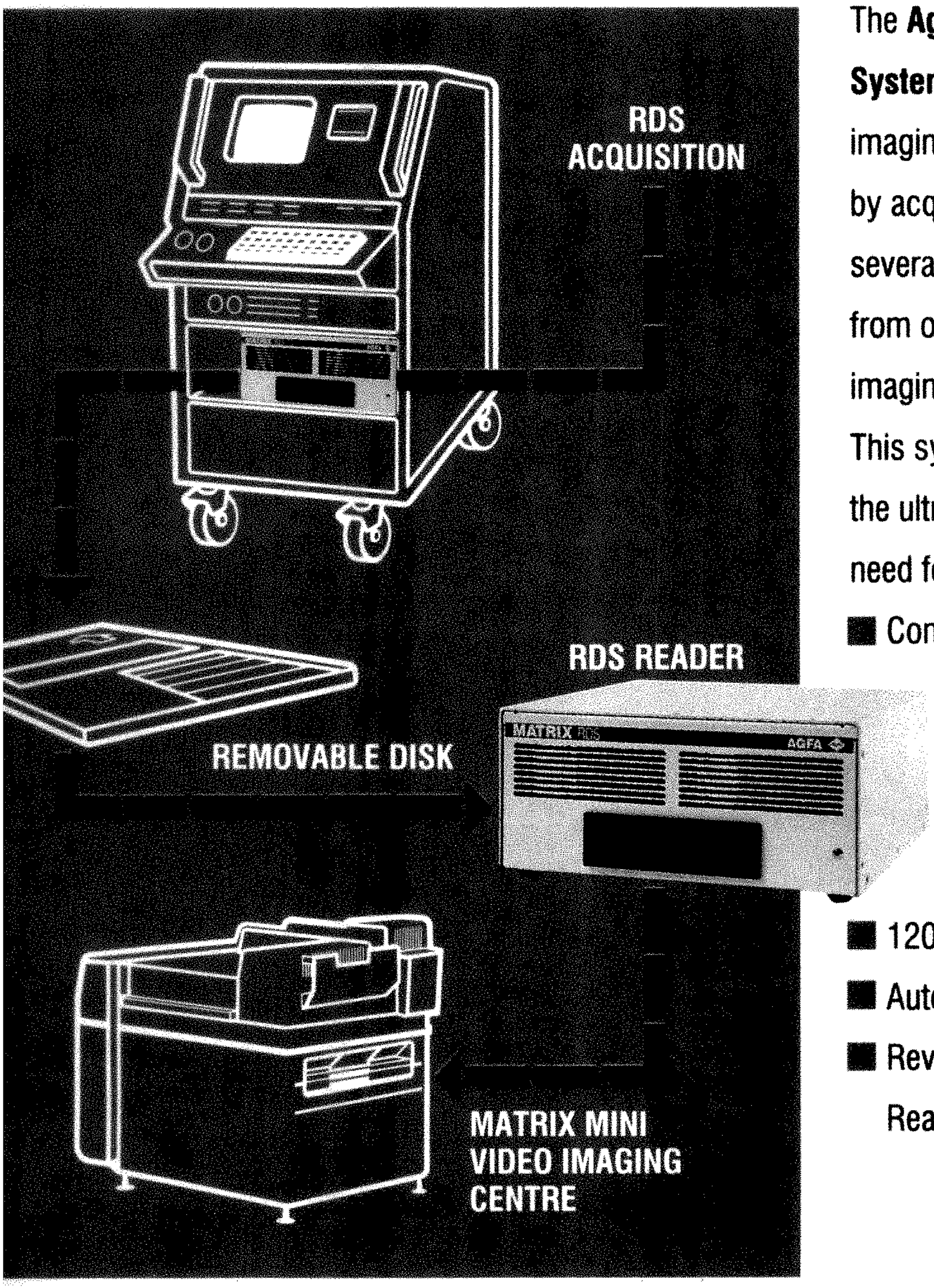

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Cholangiography in liver transplantation: a comparison of two types of biliary reconstruction

By P. Holland, FRCR, E. Morris, FRCR and *J. Buckels, FRCS

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(*Received February 1991 and in revised form June 1991*)

Keywords: Liver transplantation, Cholangiography, Biliary complications

Abstract. Orthotopic liver transplantation has been performed in Birmingham since 1982. Two types of biliary reconstruction have been used, the choledocho-choledochostomy and the choledocho-cholecysto-choledochostomy (gallbladder (GB) conduit). A retrospective study was undertaken to compare the biliary tract complications encountered at cholangiography in these two groups to assess which reconstruction is safest. In the gallbladder (GB) conduit reconstruction, the incidence of biliary leakage (20.4%) and stricture formation (14.4%), the two most serious complications, was higher than in end-to-end duct anastomosis (11% and 10%, respectively), though these differences did not reach statistical significance. This supports evidence from other centres that the choledocho-choledochostomy is the procedure of choice to minimize biliary complications. Biliary debris (14.2%) presented additional problems and was strongly associated with biliary strictures. T-tube related problems were least troublesome. The close relationship between hepatic artery occlusion and biliary complications, particularly leakage, noted in other studies is also emphasized.

Orthotopic liver transplantation is now performed in many centres around the world, but controversy remains as to the best method of biliary reconstruction. Comparisons can be made between centres that employ different reconstructions, but each centre usually prefers the use of one type only for the majority of its patients. In Birmingham, over 350 transplantations have been performed and two principal types of biliary reconstruction have been used, the choledocho-cholecysto-choledochostomy (the GB conduit) and the choledocho-choledochostomy (end-to-end donor to recipient bile duct anastomosis). All operations were performed by the same team in the same hospital, and in this study we compared the complications encountered during cholangiography in the two types of biliary reconstruction.

Patients and methods

The cholangiograms of the first 300 consecutive orthotopic liver transplantations performed at the Queen Elizabeth Hospital, Birmingham, between 1982 and 1989 were reviewed retrospectively. In total, 258 patients were transplanted (165 female, 93 male) and of these 34 received two transplants (18 female, 16 male) and four patients received three transplants (all female). The age range was 6 months to 67 years. The indications for liver transplantation are given in Table I.

Two principal methods of biliary reconstruction were used, both incorporating a latex rubber T-tube, which was used to splint the biliary anastomosis. Between 1982 and 1987, a choledocho-cholecysto-choledochostomy (GB conduit) was the preferred method of reconstruction. From 1987, a choledocho-choledochostomy (end-to-end donor to recipient bile duct anastomosis) was used whenever possible. In those patients in whom neither of these methods were suitable, a choledocho-cholecysto-jejunostomy or choledocho-jejunostomy using a Roux loop was performed.

In our centre the standard post-operative management includes a routine T-tube cholangiogram at Day 5, repeated at 3 months, just before T-tube removal.

Table I. Indications for transplantation in the 258 patients studied

Primary biliary cirrhosis	92
Acute and chronic hepatitis	51
Malignant tumours	23
Biliary atresia	19
Cryptogenic cirrhosis	17
Alcoholic cirrhosis	2
Drug-induced hepatic failure	2
Hepatic necrosis	5
Neonatal hepatitis	2
Budd Chiari (acute and chronic)	8
α-1 antitrypsin deficiency	12
Sclerosing cholangitis	19
Heart-lung-liver transplants for cystic fibrosis	3

There were single cases of erythroprotoporphyria, haemachromatosis, Wilson's disease, tyrosinaemia and a benign liver tumour.

Address correspondence to Dr P. Holland, Consultant Radiologist, X-ray Department, Alexandra Hospital, Woodrow Drive, Redditch B98 7UB.

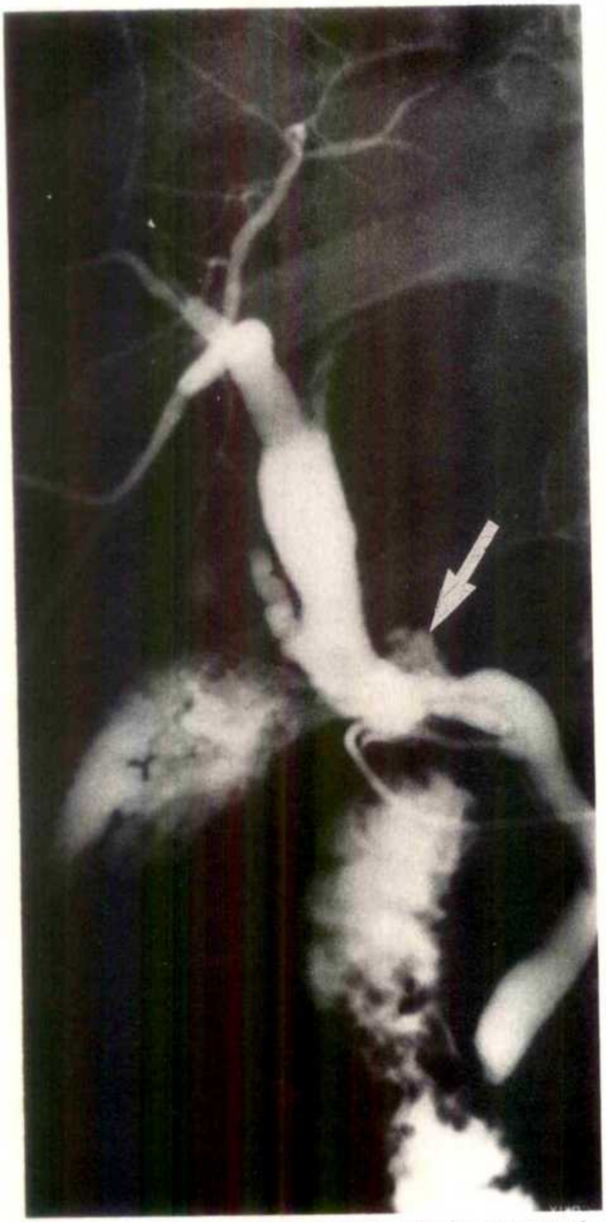

Figure 1. Choledocho-choledochostomy with an anastomotic leak (arrow).

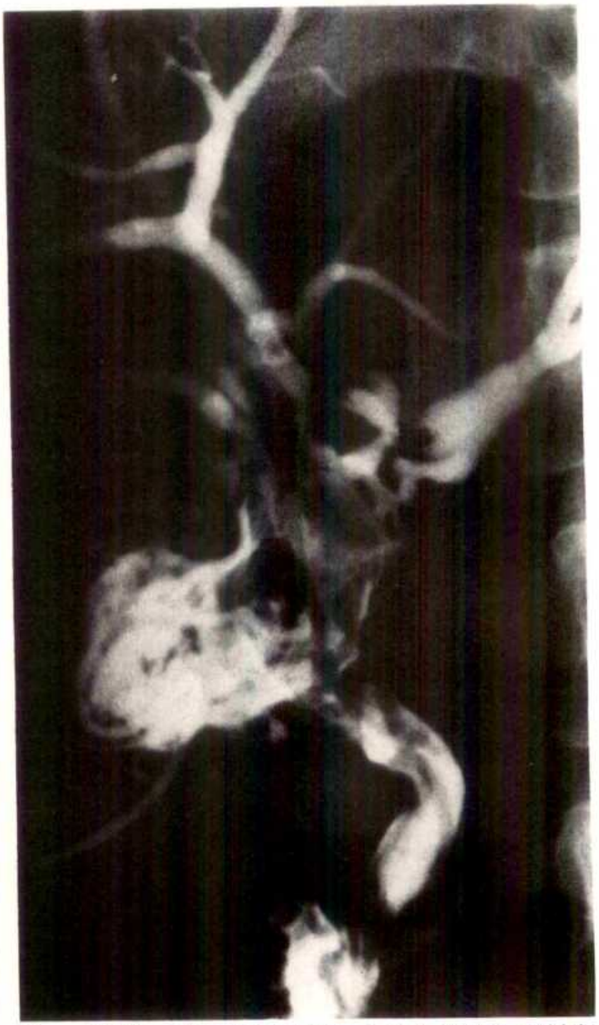

Figure 2. GB conduit demonstrating duct disruption, multiple leaks and biliary debris.

Additional cholangiography was performed as and when necessary in those patients whose clinical, biochemical or radiological findings suggested a possible underlying biliary complication. The T-tube was flushed twice daily with 10 ml of normal saline while *in situ*, a task the patients were taught to do themsleves. This was done to reduce the amount of biliary debris that might accumulate. All cholangiographic investigations were covered with an appropriate antibiotic chosen on the basis of recent sensitivities to organisms cultured from the T-tube. During cholangiography, every effort was made to fill the biliary system using gravity in preference to forceful injection so as to reduce the incidence of septicaemic episodes (Pitt et al, 1980).

Included in the review were all T-tube cholangiograms, endoscopic retrograde cholangiograms (ERC) and percutaneous transhepatic cholangiograms performed. Features noted were biliary leaks, biliary strictures with or without obstruction, debris, stones, duct irregularity, duct disruption and tube related problems. Small leaks were defined as those that had resolved on subsequent cholangiography with minimal or no treatment. Large leaks (Figs 1 & 2) were associated with extrabiliary collections and required surgical intervention and often biliary reconstruction. Strictures (Figs 3 & 4) were defined as a significant change in calibre of the bile ducts with evidence of obstruction at cholangiography. They were divided into anastomotic and non-anastomotic groups and the relationship of the T-tube limbs to the structure was noted. Not all strictures were

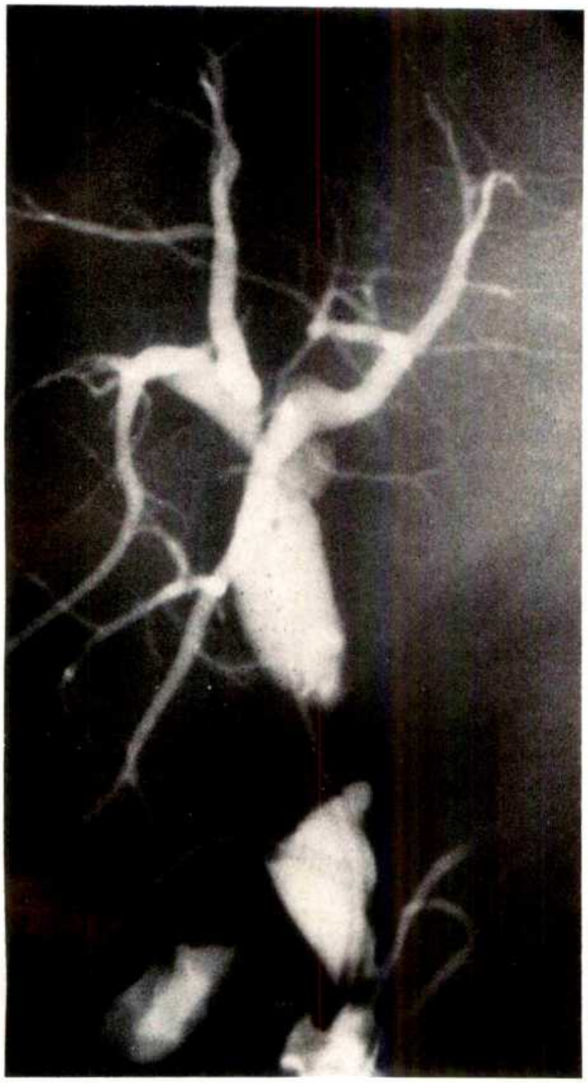

Figure 3. Choledocho-choledochostomy with an anastomotic stricture and obstruction.

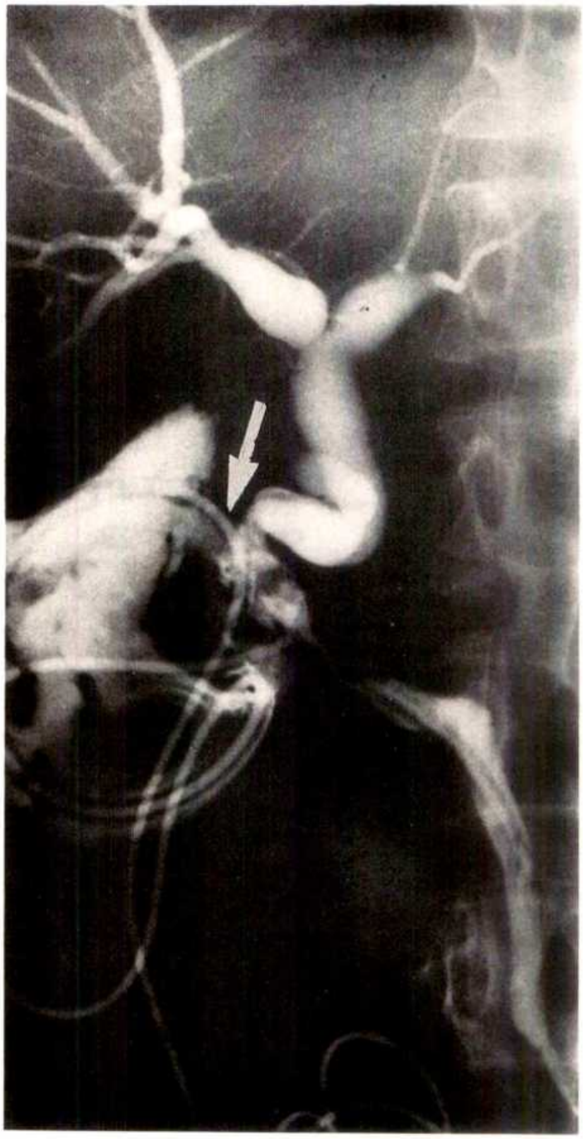

Figure 4. GB conduit with distal and proximal anastomotic strictures, and obstruction. There are bilary leaks along the T-tube tract and from the proximal anastomosis (arrow).

associated with significant obstruction following T-tube removal. The clinical notes of any patient with a complication demonstrated at cholangiography were reviewed and details of their clinical course were noted. In particular, we looked for any evidence of hepatic artery complications, episodes of rejection or other abnormalities that may be related to the biliary complication.

Results

Of the 258 patients (300 transplantations) reviewed, 41 were excluded because they had had a Roux-en-Y anastomosis (19 for biliary atresia, 17 for sclerosing cholangitis and five for other reasons). This left a group of 217 patients (252 transplantations). Of these, 62 patients (69 transplants) had no cholangiographic investigations available for review and so were also excluded. This left a study group of 155 patients, who had 183 transplantations. 83 transplantations used a gallbladder conduit anastomosis and 100 had an end-to-end duct-to-duct anastomosis. The cholangiograms of 114 transplantations were considered normal and, to our knowledge, this group have not subsequently developed a biliary complication. Therefore, 69 transplants had evidence of a biliary complication. The incidence of these expressed as a percentage of the study group of 183 transplantations is shown in Table II.

Of the 28 large leaks, 64% were associated with peribiliary or intraabdominal collections that were identified at cholangiography either using ultrasound or a

Table II. Biliary complications encountered at cholangiography in 155 patients (183 transplants) studied. The figures are expressed as a percentage of the 183 transplantations

	Complications	
	Actual number	(%)
Small leaks		
T-tube	11	(6.0)
Anastomotic	5	(2.8)
Total	16	(8.8)
Large leaks		
T-tube	7	(3.9)
Anastomotic	9	(4.9)
Non-anastomotic	—	—
Multiple	12	(6.6)
Total	28	(15.4)
Strictures		
Anastomotic	15	(8.3)
Non-anastomotic	4	(2.2)
Multiple	3	(1.6)
Total	22	(12.1)

CT scan. In many of these patients, percutaneous drainage was established before definitive surgical repair was performed. No isolated non-anastomotic leaks were identified, but in those cases where multiple leaks were observed, the disruption of the biliary system was such that the actual sites of leakage were difficult to determine, though some were undoubtedly non-anastomotic.

Biliary strictures occurred in 22 transplants (12.1%). Most were anastomotic, with four of the 22 at non-anastomotic sites and three of the 22 being multiple strictures. In nine of the 22 transplants (41%) there was significant obstruction of the biliary tract requiring biliary intervention or surgical reconstruction. In the remainder, the strictures were not associated with obstruction following T-tube removal, as confirmed by endoscopic retrograde cholangiography, biochemical monitoring or DISIDA isotope scanning. Biliary calculi were identified in six patients and all were associated with a more distal stricture.

The results were then analysed in terms of the type of biliary reconstruction used. Group I contained 83 transplants and consisted of those patients who had had a choledocho-cholecysto-choledochostomy (GB conduit). The 100 transplants in Group II had a choledocho-choledochostomy (end-to-end anastomosis). The comparative results are shown in Table III. Of note are the higher incidences of the clinically significant large leaks and of the strictures in Group I. However, chi-squared analysis of these results showed that these differences did not reach statistical significance at the $p = 0.05$ level (p was between 0.05 and 0.1).

Of the non-anastomotic strictures, those in Group I were both closely related to the position of the T-tube tip. Of those in Group II, no such relationship was noted in one, whilst the other occurred at the site of T-tube insertion. In Group I 50% of strictures were associated with obstruction after T-tube removal, compared with only 30% in Group II.

Overall, debris or inspissated bile was identified in 26 (14.2%) transplants (Fig. 5), of which 15 were in Group I and 11 were in Group II. In 20 (77%) of these patients there was co-existing biliary leakage, stricture formation or both.

Four transplants had tube related problems, namely tube migration (3) and a kinked tube (1). The latter

Table III. Comparison of biliary complications in the choledocho-cholecysto-choledochostomy and choledocho-choledochostomy groups. Figures expressed as a percentage of the transplants in each group

	Group I		Group II	
	Choledocho-cholecysto-choledochostomy (GB)		Choledocho-choledochostomy	
Small leaks				
T-tube	5	(6.0)	6	(6.0)
Anastomotic	1	(1.2)	4	(4.0)
Total	6	(7.2)	10	(10.0)
Large leaks				
T-tube	5	(6.0)	2	(2.0)
Anastomotic	5	(6.0)	3	(3.0)
Non-anastomotic	—	—	—	—
Multiple	7	(8.4)	6	(6.0)
Total	17	(20.4)	11	(11.0)
Strictures				
Anastomotic	8	(9.6)	7	(7.0)
Non-anastomotic	2	(2.4)	2	(2.0)
Multiple	2	(2.4)	1	(1.0)
Total	12	(14.4)	10	(10.0)

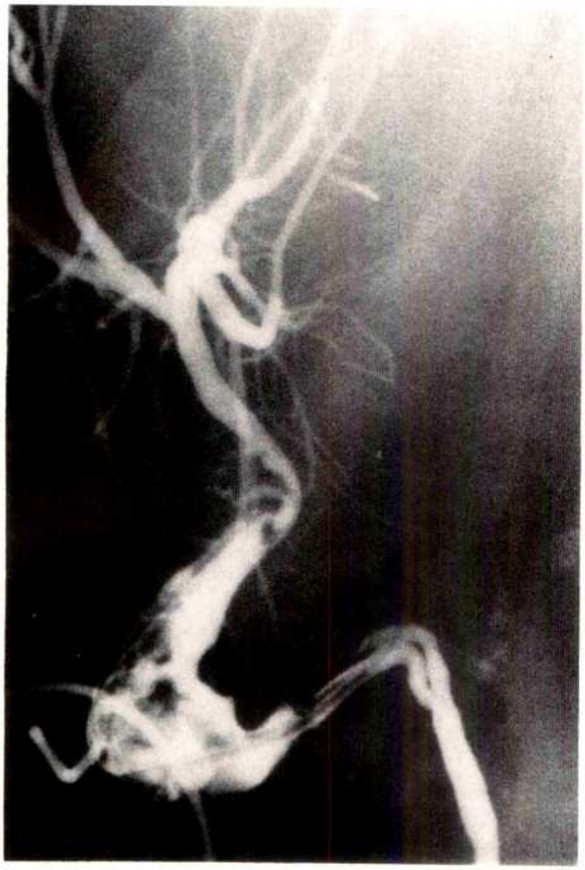

Figure 5. GB conduit with biliary debris within the conduit itself.

caused obstruction within the biliary tract until it was removed. In none of these patients was there a biliary problem after the T-tube was removed.

In those patients with biliary debris, a leak, or a stricture, a possible relationship between the complication and episodes of rejection, or an hepatic artery complication was sought by reviewing the patients subsequent clinical course. This group comprised of 47 patients (27 in Group I, 20 in Group II). In 25 cases no such cause for the post-operative complication could be identified. The results of the remaining 22 patients are shown in Table IV. Overall, 11 out of 22 biliary complications were associated with acute rejection episodes, as indicated by liver biopsy and response to increased immunosuppression. Seven out of the 22 were associated with hepatic artery complications (occlusion, stenosis or aneurysm). In four patients, both rejection and arterial complications were found. No definite relationship between strictures and chronic rejection was noted.

Discussion

Since the first human liver transplantation in 1963 (Starzl et al, 1963) the life expectancy of patients has improved, mainly as a result of better patient selection, refined organ procurement and preservation, meticulous surgical grafting techniques, the introduction of cyclosporin and improved post-operative management (Dominguez et al, 1986). This has resulted in substantial improvement in results from all centres. Despite this, biliary tract complications remain a major cause of post-transplantation morbidity. Ultrasound is useful in detecting biliary obstruction, though its reliability in excluding other biliary complications is poor (Zemel et al, 1988). Biliary scintigraphy provides an excellent means of differentiating obstruction from other causes of cholestasis (Lecklitner et al, 1986; Lee et al, 1986; Loken et al, 1986), but may also be unreliable at identifying leakage. Therefore, direct visualization of the biliary tract using tube cholangiography, percutaneous cholangiography or ERC remains the most accurate means of diagnosing a biliary tract problem (Zajko et al, 1985).

Table IV. Biliary complications in which possible aetiological factors can be identified in 22 patients

	Complication		
	Leak	Stricture	Debris
Aetiology			
Rejection	10	6	2
Arterial complications	9	1	1

In seven of these patients more than one possible cause was identified. In 25 patients no cause was found.

Many techniques for biliary reconstruction have been used and debate still exists as to the most appropriate procedure. Choledocho-choledochostomy is popular and reported complication rates, usually expressed in terms of significant biliary leaks and strictures, vary from 17% to 48% (Iwatsuki et al, 1983; Neuhaus et al, 1984; Krom et al, 1985; Lerut et al, 1987). Overall, 21% of the transplants in our choledocho-choledochostomy series developed a complication using these criteria, comparing favourably with other results.

The gallbladder conduit was considered an important development in the early years of liver transplantation when biliary leakage was a major cause of morbidity and mortality. Despite this, the choledocho-cholecysto-choledochostomy (GB conduit) has been little used in most centres other than our own and the Cambridge/King's College Hospital programme (Evans et al, 1990). The Cambridge/King's group identified biliary complications in 76 out of 148 (41%) of a series of transplants where a post-operative problem was suspected and cholangiography consequently performed. The commonest abnormality was biliary stricture formation (63%), with bile leakage present in only 18%. Halff et al (1989) similarly noted a high incidence of complication with the GB conduit (50%), though this reconstruction was used in only 10 of over 2000 transplantations. In this study, we demonstrated significant leaks and strictures in 35% of the GB conduit group. We believe that in our centre, the almost unique situation of having two large groups of alternative biliary reconstructions performed by the same team allowed us to compare reliably the two procedures. We accept that the retrospective, non-randomized nature of the study, together with improvements in transplantation technique over the 8 year study period, may make interpretation of findings related to the earlier gallbladder conduit group more difficult. Allowing for this, and although the differences between complication rates in the choledocho-choledochostomy and GB conduit groups did not reach statistical significance, we feel that the choledocho-choledochostomy should be the procedure of choice whenever possible.

Biliary leakage in the immunosuppressed patient is a serious complication (Rolles, 1987) and in our experience was the most frequent in both types of reconstruction. Many of the small leaks, and a number of unsuspected large leaks, were discovered at routine cholangiography. To what extent early diagnosis altered morbidity is not known, but frequent cholangiographic review or speedy surgical intervention probably prevented more serious sequelae developing. No appreciable differences were seen regarding the site of leakage between the two types of reconstruction. No solitary non-anastomotic leak was identified, though several were seen in the 13 cases of multiple biliary leaks (or duct disruption). Of these cases, six were associated with hepatic artery occlusion and four with allograft rejection, emphasizing the close association of biliary abnormalities with vascular complications (Zajko et al, 1987). Ultrasound as a screen for biliary leakage is unreliable, despite the fact that most leaks are associated with peribiliary or intrahepatic collections (Zemel et al, 1988).

Although the rate of stricture formation was higher in the GB conduit reconstruction, our experience did not reflect the findings of Evans et al (1990), who demonstrated strictures in 63% of their cases, over half of which were non-anastomotic in site. They identified a number of strictures that appeared to be related to the position of the T-tube limbs; we could identify only two cases (both GB conduits) in which this association was possible. We did, however, note that a large number (56.5%) of strictures identified at cholangiography did not demonstrate evidence of biliary obstruction following T-tube removal, underlining the role that the T-tube plays in obstruction whilst *in situ*. In addition, numerous cases were seen of biliary debris or inspissated bile complicating and adding to the obstruction of the biliary tree at the stricture level. The high coexistence of biliary debris with stricture formation suggests a mechanical aetiological factor (Starzl et al, 1977), though bile composition changes said to occur in post-transplant patients may play a part (Waldram et al, 1975). There is also evidence that the two complications may have a common ischaemic aetiology (McMaster et al, 1978). In several patients without a stricture, inspissated bile proved to be a problem after T-tube removal and, for these, endoscopic papillotomy and balloon catheter removal of the debris was very successful.

The relationship that exists between biliary complications, vascular complications and episodes of rejection is still not clear. Certainly hepatic artery occlusion is associated with both biliary leakage and stricture formation (Zajko et al, 1987), and may also be related to acute rejection (White et al, 1987), though which occurs first is not certain. Doppler ultrasound as a screening examination of the hepatic vessels is sensitive and accurate (Segel et al, 1986; Flint et al, 1988) and provides a means of selecting patients who require arteriography. Likewise, cholangiographic changes may provide evidence supporting the need for angiography (Zajko et al, 1987) or liver biopsy (Bauman et al, 1989) in the evaluation of hepatic dysfunction after transplantation. Of the 47 patients in this study with a serious biliary complication, 26 had a possible aetiological cause identified, the strongest association being between leakage and both rejection and hepatic artery occlusion.

In conclusion, when comparing complications identified at cholangiography in two principal types of biliary reconstruction used during liver transplantation within the same centre, it seems that the choledocho-choledochostomy should be the procedure of choice.

Acknowledgments

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Is a short femur length a useful ultrasound marker for Down's syndrome?

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Keywords: Down's syndrome, Femur length, Ultrasound marker

Abstract. To assess the significance of a short femur in the antenatal diagnosis of Down's syndrome a retrospective analysis was made of all Down's syndrome fetuses diagnosed over a 3 year period. 11 fetuses were found to have had a biparietal diameter and femur length measurement taken between 15 and 24 weeks gestation. Normal graphs were plotted for femur length against gestational age, femur length against biparietal diameter and biparietal diameter/femur length against gestational age. When the Down's syndrome measurements were plotted on the normal graphs there were four abnormal measurements. These four measurements, however, represented two fetuses both of which demonstrated other abnormalities, one cystic hygroma and one duodenal atresia with choroid plexus cysts. We do not feel that the femur length measurement is useful in the antenatal diagnosis of Down's syndrome.

There has been considerable debate over the significance of a short femur length in the antenatal diagnosis of Down's syndrome. A number of authors have found the femur to be significantly shortened in fetuses with Down's syndrome (Benacerraf et al, 1987; Lockwood et al, 1987; Perella et al, 1988; Brumfield et al, 1989; Cuckle et al, 1989; Dicke et al, 1989). Later papers, however, have shown little or no difference in the length of the femur in Down's syndrome fetuses compared with normal fetuses (Winston & Horger, 1988; La Follette et al, 1989; Lynch et al, 1989; Peters et al, 1989; Marquette et al, 1990; Nyberg et al, 1990). In order to address this problem, a retrospective study was made of all Down's syndrome fetuses diagnosed at Queen's Medical Centre, Nottingham.

Materials and methods

Over a 3 year period a retrospective study was carried out on all Down's syndrome fetuses diagnosed either by amniocentesis or postnatal karyotyping. 21 fetuses were identified, but on reviewing the antenatal scans only 11 fetuses had both biparietal diameter and femur length measurements carried out between 15 and 24 weeks gestation. The biparietal diameter was measured as the transverse diameter of the fetal head at the level of the thalami. The femur length was determined from the longest single measurement.

Using measurements from 425 normal pregnancies graphs were plotted for

(a) femur length against gestational age

$$\text{fitted line} = \text{fl} = 0.018928\,\text{ga}^{2.8908}\exp(-0.060148\,\text{ga})$$

where fl = femur length and ga = gestational age.

(b) Femur length against biparietal diameter

fitted line of form =

$$\sqrt{\text{fl}} = b\sqrt{\text{BPD} - 11.2128} + a$$

where fl = femur length and BPD = biparietal diameter.

(c) Biparietal diameter/femur length against gestational age

$$\text{fitted line} = \text{BPD/FL} = p6 + p5\,\text{ga}^5 + \ldots\; p2\,\text{ga}^2 + p1\,\text{ga}$$

where BPD = biparietal diameter, fl = femur length, ga = gestational age, $p6 = 16.908$, $p5 = -0.71113 \times 10^{-6}$, $p4 = 0.10483 \times 10^{-3}$, $p3 = -6.1609 \times 10^{-3}$, $p2 = 0.18048$ and $p1 = 0.10572 \times 10^{3}$.

The normal ranges were calculated as mean plus or minus two standard deviations (SD). In the case of the femur length against the biparietal diameter graph, 95% and 99% tolerance ellipses were calculated for the bivariate distribution of biparietal diameter against femur length.

The measurements of the Down's syndrome fetuses were then plotted on the normal graphs. All measurements were carried out by four experienced sonographers using modern ultrasound equipment (IGE RT 3600, Hitachi EUB 410 and Hitachi EUB 450).

Results

When the measurements from the Down's syndrome fetuses were plotted on the graphs from normal fetuses there were four abnormal results. One fetus had an abnormal measurement on the femur length against gestational age graph (Fig. 1). One measurement fell

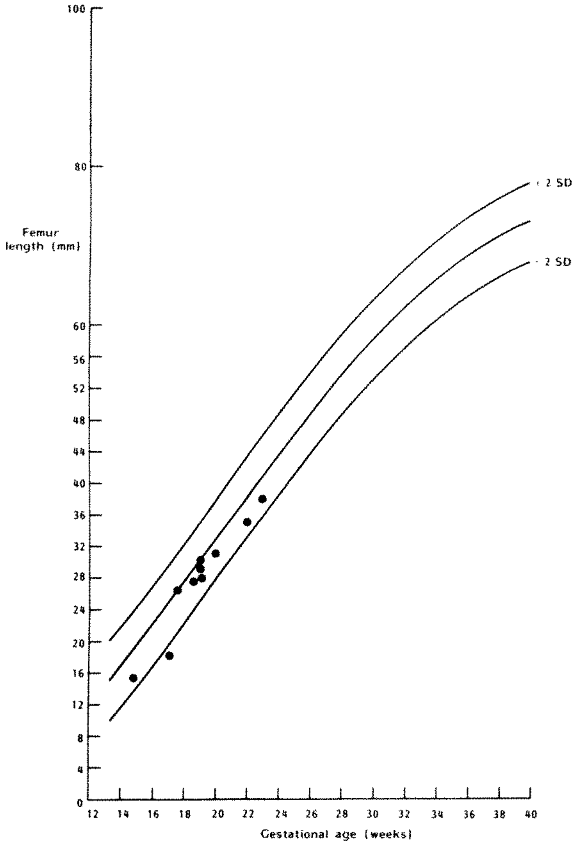

Figure 1. Femur length against gestational age. The closed circles represent Down's syndrome fetuses.

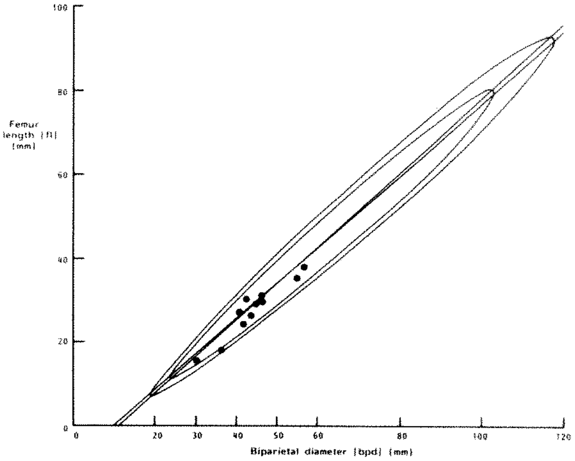

Figure 2. Femur length against biparietal diameter. The closed circles represent Down's syndrome fetuses.

outside the 95% limit in the femur length against the biparietal diameter graph (Fig. 2). Two fetuses were abnormal on the biparietal diameter/femur length against gestational age graph (Fig. 3). These four abnormal results, however, represented two fetuses both of which demonstrated other abnormalities, one fetus showing a cystic hygroma and the second showing choroid plexus cysts with the subsequent development of duodenal atresia.

Discussion

The role of the short femur length in the antenatal diagnosis of Down's syndrome has been evaluated by many investigators. In a retrospective study Lockwood et al (1987) found femur lengths significantly shorter in Down's syndrome fetuses. However, their data were taken from patients undergoing amniocentesis, and therefore a high risk population. A similar criticism can be made of the paper by Benaceraff et al (1987) which produced a simple linear regression model of the relation between femur length and biparietal diameter. (Expected femur length $= -9.645 + 0.9338 \times \mathrm{BPD}$.) They found a ratio of actual to expected femur length of 0.91 or less, and detected 68% of fetuses with Down's syndrome. We applied this model to our own data and at the 0.91 cut off, 82% of the Down's syndrome fetuses were detected but this level also selected 34% of our normal population. At the lower cut off of 0.87 we would have detected 64% of our Down's syndrome fetuses but also 13% of the normal population. Clearly this model cannot be applied to a low risk population.

In addition, Perella et al (1988) were able to detect only 26% of Down's syndrome fetuses using the 0.91 cut off level. Brumfield et al (1989) studied 15 fetuses with Down's syndrome, finding that a biparietal

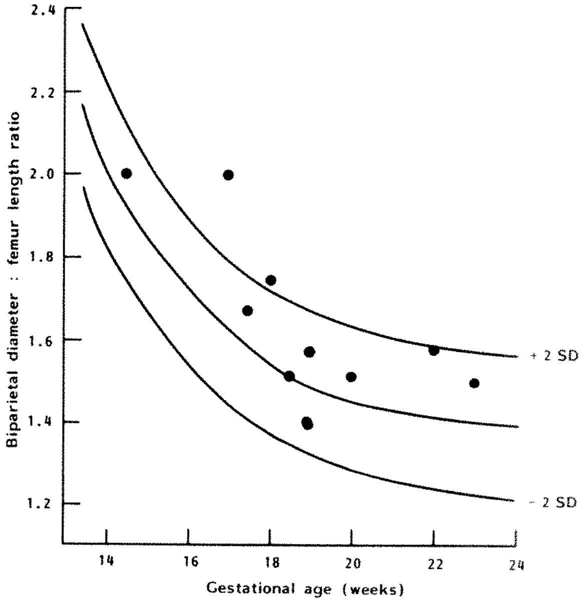

Figure 3. Biparietal diameter/femur length against gestational age (95% and 99% tolerance ellipses for the bivariate distribution of biparietal diameter/femur length). The closed circles represent Down's syndrome fetuses.

diameter/femur length ratio of 1.8 or more predicted 40% of Down's syndrome fetuses. When we applied this figure to our own data only two (19%) Down's syndrome fetuses were detected.

A number of papers found that the femur length was not useful in the diagnosis of Down's syndrome. Winston and Horger (1988) found no difference in femur length between 10 fetuses with Down's syndrome and 74 control pregnancies. La Follette et al (1989) were also unable to demonstrate a difference in femur length between their control population and Down's syndrome fetuses.

Lynch et al (1989) studied 11 twin pregnancies in which one twin had Down's syndrome. They found that neither the biparietal diameter/femur length ratio or the actual to expected femur length ratio were useful in distinguishing the normal from the abnormal twin. Three further papers have also found the femur length of little use in the detection of Down's syndrome (Peters et al, 1989; Marquette et al, 1990; Nyberg et al, 1990).

It seems that the early papers used high risk populations and models which cannot be applied to our data. In addition, there are a mounting number of papers showing that femur length is of little use in the detection of Down's syndrome. Finally, using standard graphs we were unable to detect Down's syndrome using the femur length as a marker.

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Late enhancement of the left ventricular wall in hypertrophic cardiomyopathy by ultrafast computed tomography: a comparison with regional myocardial thickening

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Keywords: Hypertrophic cardiomyopathy, Left ventricle, Regional wall thickening, Computed tomography

Abstract. Eight patients with hypertrophic cardiomyopathy (HCM) were examined by ultrafast computed tomography (UFCT) to investigate the relationship between late enhancement (LE) of the left ventricular (LV) wall after injection of contrast medium and the variations between minimum and maximum wall thickness of the LV. Late enhancement was usually found as a patchy, stained area in the myocardium on delayed phase volume mode images of UFCT. Out of 48 LV segments of the patients with HCM, 21 had LE. Normalized percentage regional wall thickening in the segments that had LE was significantly less than that in the segments that did not have LE (63.6±44.5% and 137.6±54.6%, respectively; $p < 0.001$). This may reflect abnormal myocardial architecture.

With ultrafast computed tomography (UFCT), late enhancement (LE) and early defect (ED) of the left ventricular (LV) wall after an injection of contrast medium were abnormal myocardial findings (Naito et al, 1990b). One of these, LE, was also found in patients with hypertrophic cardiomyopathy (HCM) (Fig. 1). However, there was little evidence of the relationship between LE and abnormal myocardial architecture in patients with HCM.

A recent report has shown that LV myocardial lesions, such as myocardial hypertrophy, myocardial disarray and fibrosis, affected the LV contractile dynamics in patients with HCM (Usuki et al, 1989). The purpose of this report is to investigate the relationship between LE of the LV wall and the change between minimum and maximum wall thickness of the LV in patients with HCM.

Materials and methods

Patients

After obtaining informed consent, eight patients diagnosed clinically as having HCM (four females, four males, mean age 32.5 years; Table I) and eight patients without any disease causing cardiac hypertrophy or abnormality of the LV wall contraction (two females, six males, mean age 35.6 years) were examined. The diagnosis of HCM was made mainly by echocardiography. Of unknown cause, HCM is characterized by disproportionate hypertrophy of the LV and occasionally also of the right ventricle (RV) (WHO/ISFC, 1980). Two patients had hypertrophic obstructive cardiomyopathy and six had hypertrophic non-obstructive cardiomyopathy.

Ultrafast computed tomography scanner

The scanner used is the ultrafast CT C-100 (Imatron, USA), with an electron beam scan mechanism. The

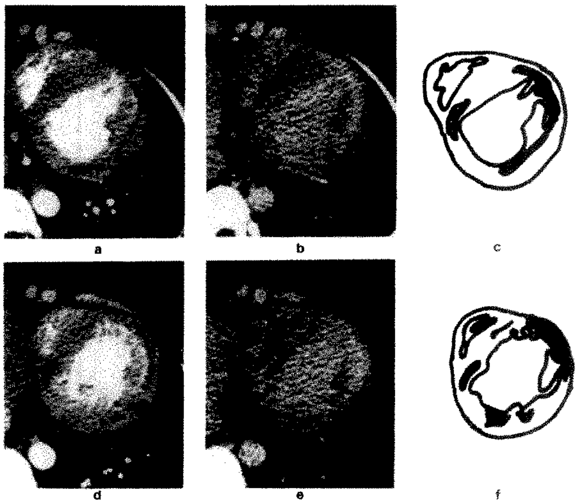

Figure 1. 21-year-old woman with hypertrophic non-obstructive cardiomyopathy. (a, d) Early phase volume mode images of UFCT; (b, e) delayed phase images of the same levels as (a) and (d), respectively. (c, f) Diagrams of late enhancement.

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Table I. Details of patients

	Case no.							
	1	2	3	4	5	6	7	8
Age (years)	43	13	17	52	21	13	57	44
Sex	F	M	F	M	F	M	F	M
Family history	–	–	–	–	–	–	–	–
Type of HCM	HOCM	HNOCM	HNOCM	HOCM	HNOCM	HNOCM	HNOCM	HNOCM
Symptoms								
dyspnoea	+	–	–	+	+	–	–	–
chest pain	–	–	+	–	+	–	–	–
dizziness	+	–	–	+	–	–	–	–
Heart sounds								
IIIrd sound	–	–	–	–	+	–	+	–
IVth sound	+	+	–	+	+	+	–	+
systolic murmur	+	+	–	+	–	–	–	–
Chest radiograph								
CTR > 50%	–	–	–	–	+	–	+	–
Electrocardiogram								
LV hypertrophy	+	+	–	+	+	–	+	+
abnormal Q	+	+	–	+	–	–	–	+
ST-T change	+	–	+	+	+	+	+	+
Echocardiogram								
thickness (mm)								
septal wall	17	16	11	21	13*	18	25	23
posterior wall	13	9	8	10	13*	10	11	12
mitral valve								
SAM	+	+	–	+	–	–	+	+
MR	+	–	–	+	+	+	–	+

HCM: hypertrophic cardiomyopathy; HOCM: hypertrophic obstructive cardiomyopathy; HNOCM: hypertrophic non-obstructive cardiomyopathy; CTR: cardiothoracic ratio; LV: left ventricle; SAM: systolic anterior movement; MR: mitral regurgitation. *Entire wall thickening.

X-ray source is comprised of a single scanning electron beam (130 kV, 600 mA) that is magnetically focused and deflected onto four semicircular (210°) tungsten target rings. X rays are detected in a stationary double array of scintillation-photodiode crystals, one containing 864 and the other 432. With successive scans, up to eight slices of 8 mm thickness can be acquired in rapid sequence. Each target ring is separated by 4 mm distance.

The irradiation dose of the 50 and 100 ms scans of UFCT is about one-tenth and one-fifth, respectively, of the conventional scan of the CT/T8800 scanner (General Electric Co., USA) (Saito et al, 1990).

In the ciné mode, images are acquired at 50 ms intervals with an 8 ms interscan delay or a scanning speed of 17 images/s. Thus, for heart rates of 50–100 beats/min, a complete cardiac cycle can be imaged with a four-level (20 frames/level) film. For heart rates of 100 beats/min or greater, a complete cardiac cycle can be imaged with an eight-level (10 frames/level) film. No table incrementation is needed for ciné mode study. In this mode, electrocardiogram (ECG) triggering is usual.

The volume mode of the UFCT uses table incrementation. One of four target rings is used. Electrocardiogram-triggered 100 ms scans are commonly used in cardiac examinations, and up to 20 contiguous images of 6 mm thickness covering the entire heart are obtained within 30–40 heart beats.

The scanner has no moving gantry, but its scan table can slew 25° in each horizontal direction with a downward tip of 25°. Oblique views of the LV on the short axis are possible (Rees et al, 1986).

Scanning and experimental protocol

Each patient was positioned supine on the movable table, with the head directed towards the gantry, and then connected to an electrocardiographic monitor integrated with the scanner for continuous recording of heart rate. A non-ionic low-osmolar contrast medium, iopamidol (370 mgI/ml), was injected into the antecubital vein by a power injector.

The positioning of the patient for the short-axis views was calculated from the angle of the heart derived from each patient's postero-anterior chest radiograph. No table tip was used in this study. Therefore, the exact short-axis position was not used in this study. We called the position used in our study "the near short-axis position".

Three sets of the near short-axis volume mode images were obtained for each patient. The plain (without contrast medium) UFCT volume mode images were recorded first. Early phase volume mode images of

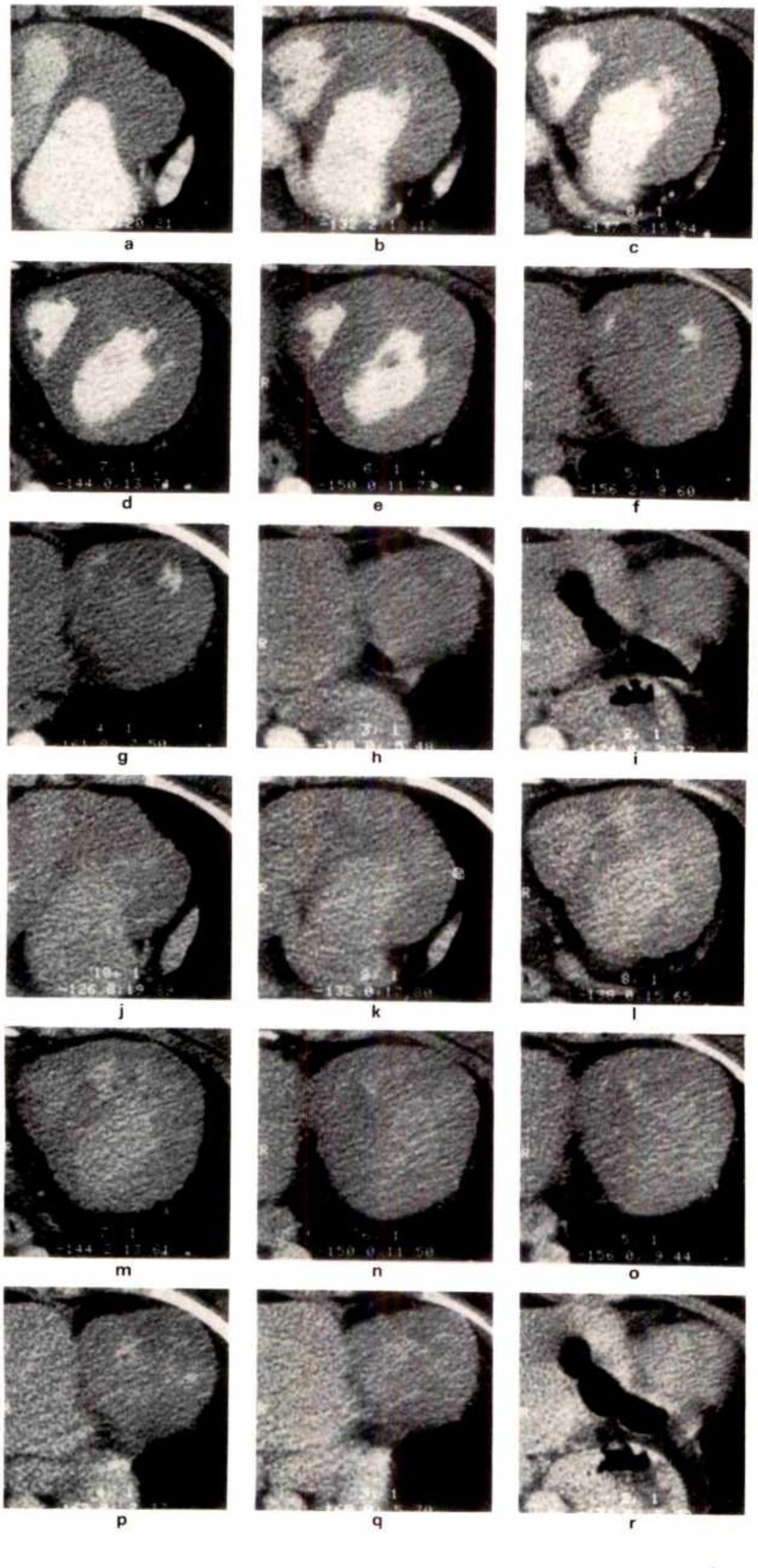

Figure 2. 17-year-old woman with hypertrophic non-obstructive cardiomyopathy. (a–i) are nine out of 10 early phase volume mode images of UFCT; (j–r) are the delayed phase images of the same levels as (a–i). Late enhancement was found as a patchy stained area in the myocardium on the delayed phase volume mode UFCT images.

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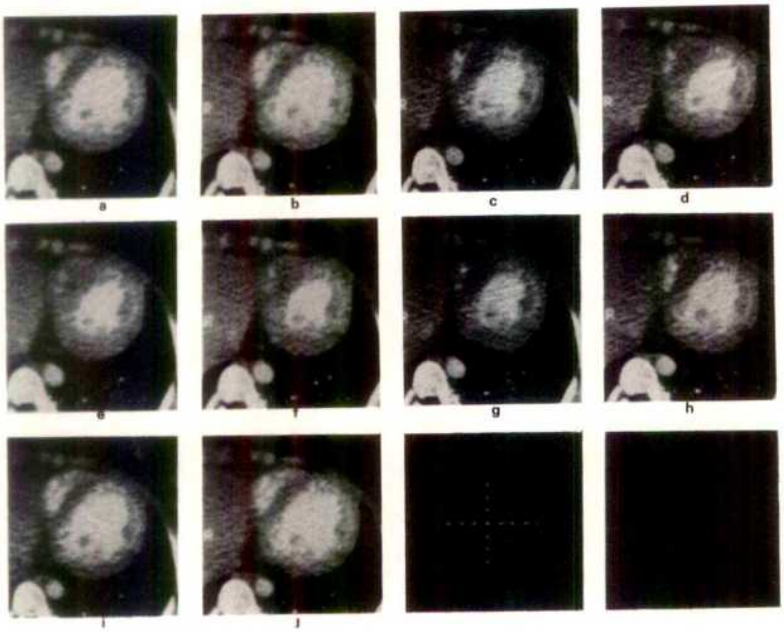


Figure 3. Ten contiguous images of the same level of an eight-level, 10 images/level, near short-axis ciné mode scan; (a) and (g) were identified as end-diastole and end-systole, respectively.

contrast enhancement were then obtained 25–60 s after the start of an injection, and the delayed phase volume mode images were obtained 4–5 min from the start of the contrast medium injection (Fig. 2). The injection volume and rate of the contrast medium were 60 ml and 1.5 ml/s, respectively, and this ensured opacification of the LV and RV throughout the duration of early phase images. The slice thickness and the table incrementation were 6 mm and 10 mm. Scans were obtained from the apex to the base of the LV in the near short axis in each set. Ten contiguous sections were required to image the entire LV. Each scan was triggered just after 40% of the RR-interval from the R-wave of the ECG.

Near short-axis ciné mode scans were then made to assess myocardial wall thickness. The table was adjusted so that the most cranial portion of the LV wall was included in the most cranial level. An eight-level, 10 images/level ciné mode was obtained. The injection volume and rate of the contrast medium were 30 ml and 1 ml/s, respectively, ensuring opacification of the LV and RV throughout the scan. Each scan was triggered at the R-wave of the ECG (Fig. 3).

Patients breathed normally during the procedures.

Analysis of UFCT images

We measured the mean CT value of the LV cavity and CT values of the LV myocardium on the plain volume mode images of UFCT [CT(cp) and CT(mp)] and on the delayed phase images [CT(cd) and CT(md)]. The percentage rise of myocardial CT values (%RMCT) was then calculated as:

$$\%\text{RMCT} = \frac{\text{CT(md)} - \text{CT(mp)}}{\text{CT(cd)} - \text{CT(cp)}} \times 100$$

An area of LE was defined as that LV myocardial area where %RMCT was over 80% (Figs 1 and 2).

In ciné mode images, the endocardial and epicardial borders of the LV myocardium were outlined with a track-ball cursor for each anatomical level and for each time. Computer-generated radii were placed counterclockwise every 30°. An epicardial centroid was used for the origin of the radii. Using these radii, we determined six segments (every 60°) of the LV myocardium (Fig. 4). The window width and level of the UFCT images were fixed at 400 and 40, respectively. The papillary muscles of the LV were included in the ventricular volume. End-diastolic time was identified as the time with the maximal LV volume. End-systolic time was identified as the time with the minimal LV volume. In the analysis of the change of the regional LV wall thickness, we used the level which gave the largest LV cavity area in the end-diastolic time images. The myocardial wall thicknesses at the end-diastole [CT-thickness (d)] and at the end-systole [CT-thickness (s)] were measured at the centre of each segment along the radii. The percentage regional wall thickening (%RWT) of each segment was then calculated as:

$$\%\text{RWT} = \frac{\text{CT-thickness (s)} - \text{CT-thickness (d)}}{\text{CT-thickness (d)}} \times 100$$

Since the %RWT in the anterior and lateral segments of the normal controls were larger than those in the posterior and septal segments (Table II), the %RWT of each wall segment in patients with HCM was normalized by the mean value for patients without disease causing cardiac hypertrophy and with no abnormality of LV wall contraction. The normalized %RWT

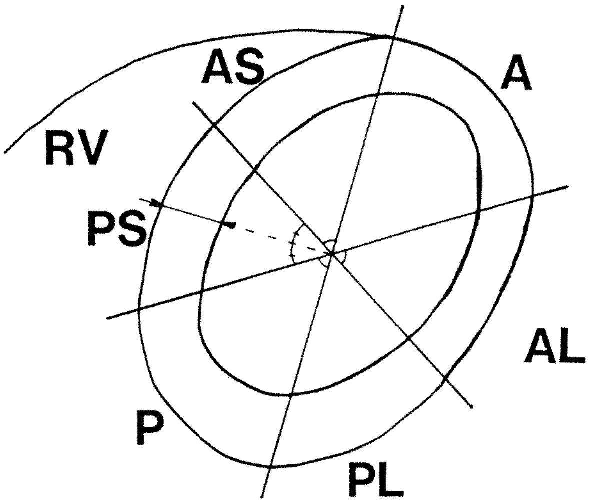


Figure 4. The LV myocardium was divided into six segments in the near short-axis ciné mode images. The myocardial wall thicknesses were measured at the centre of each segment. PS = postero-septal, AS = antero-septal, A = anterior, AL = antero-lateral, PL = postero-lateral and P = posterior segments.

Table II. Mean values of the myocardial wall thicknesses at the end-diastole [CT-thickness (d)], the end-systole [CT-thickness (s)], and the percentage regional wall thickening (%RWT) of eight controls on short-axis ciné mode study of UFCT

Segments	CT-thickness (d) [mm]	CT-thickness (s) [mm]	%RWT
Anterior	5.5	11.3	105.5
Antero-lateral	7.7	13.8	79.2
Postero-lateral	8.2	14.8	80.5
Posterior	7.4	10.7	44.6
Postero-septal	10.8	15.4	42.6
Antero-septal	8.2	13.1	59.8

(%NRWT) was used as a parameter of the regional LV wall contractile function. The %NRWT for each wall segment was calculated as:

$$\%\text{NRWT} = \frac{\%\text{RWT in each patient}}{\text{mean }\%\text{RWT in controls}} \times 100$$

The normalized percentage end-diastolic and end-systolic wall thicknesses (%NDWT and %NSWT, respectively) for each wall segment were also calculated as:

$$\%\text{NDWT} = \frac{\text{CT thickness (d) in each patient}}{\text{mean CT thickness (d) in controls}} \times 100$$

$$\%\text{NSWT} = \frac{\text{CT thickness (s) in each patient}}{\text{mean CT thickness (s) in controls}} \times 100$$

Computed tomographic images were analysed independently by two observers in all cases.

Statistical analysis was achieved by a Welch's test. Data were expressed as mean ±SD.

Results

Late enhancement was usually seen as a patchy, stained area in the myocardium on delayed phase volume mode UFCT images. Out of 48 segments of patients with HCM, 21 had LE.

The %NDWT in the segments with LE was significantly larger than that in the segments without LE [199.0±72.6% and 104.4±43.2%, respectively; $p < 0.001$; Fig. 5(a)].

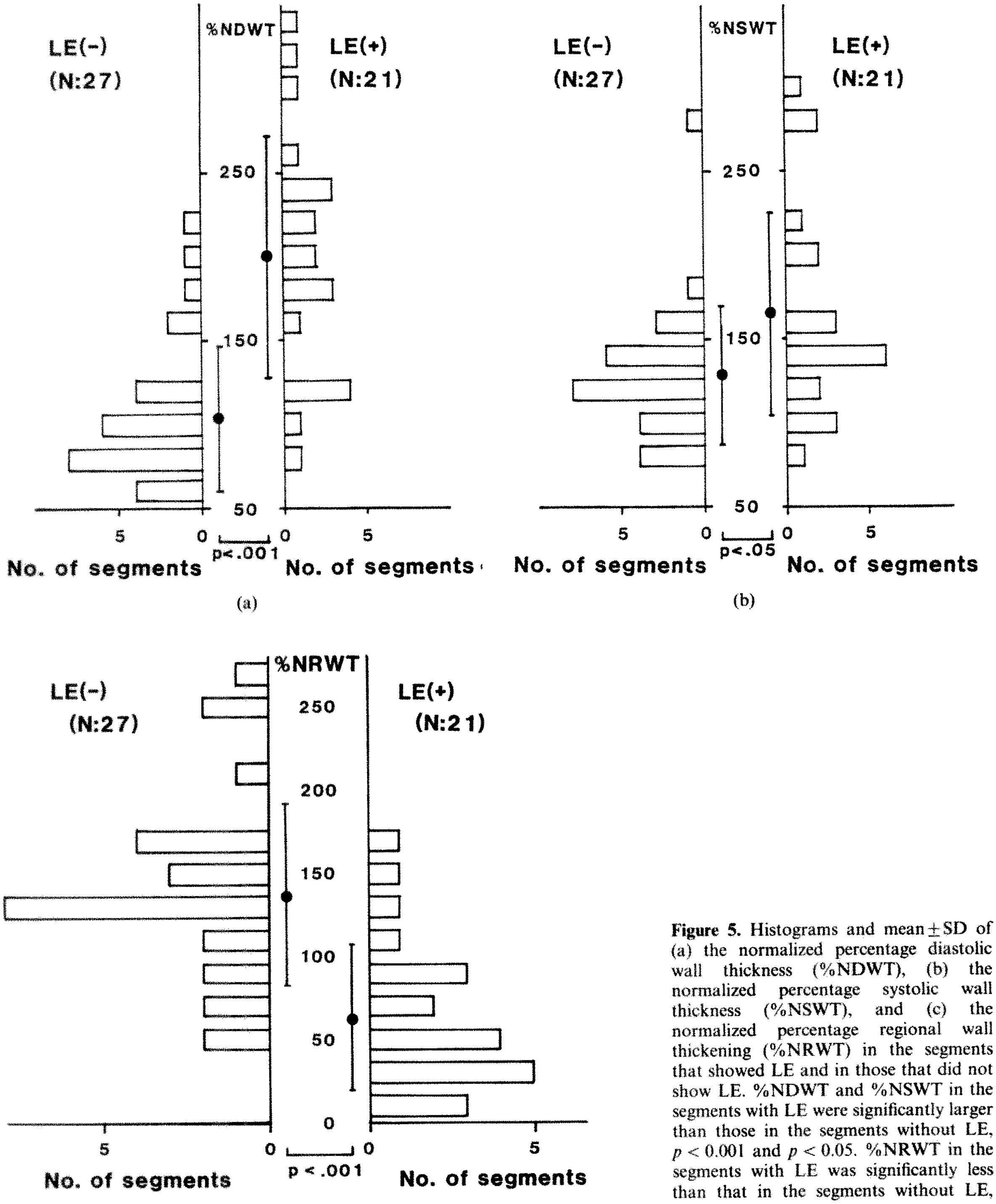
The %NSWT in the segments with LE was larger than that in the segments without LE [164.7±61.1% and 127.8±41.4%, respectively; $p < 0.05$; Fig. 5(b)].

The %RWT in the segments with LE was significantly less than that in the segments without LE (23±18% and 50±16%, respectively; $p < 0.001$; Table

Table III. Mean±SD of percentage regional wall thickening (%RWT) in left ventricular wall segments with LE and in those without

Segment	LE(−)			LE(+)		
	No. of segments	%RWT		No. of segments	%RWT	
		Mean	SD		Mean	SD
Anterior	4	52	14	4	43	23
Antero-lateral	7	60	11	1	38	
Postero-lateral	6	57	6	2	26	12
Posterior	5	38	16	3	20	11
Postero-septal	2	44	18	6	13	10
Antero-septal	3	34	16	5	16	10
Total	27	50*	16	21	23*	18

*Statistically significant at $p < 0.001$.



(a)

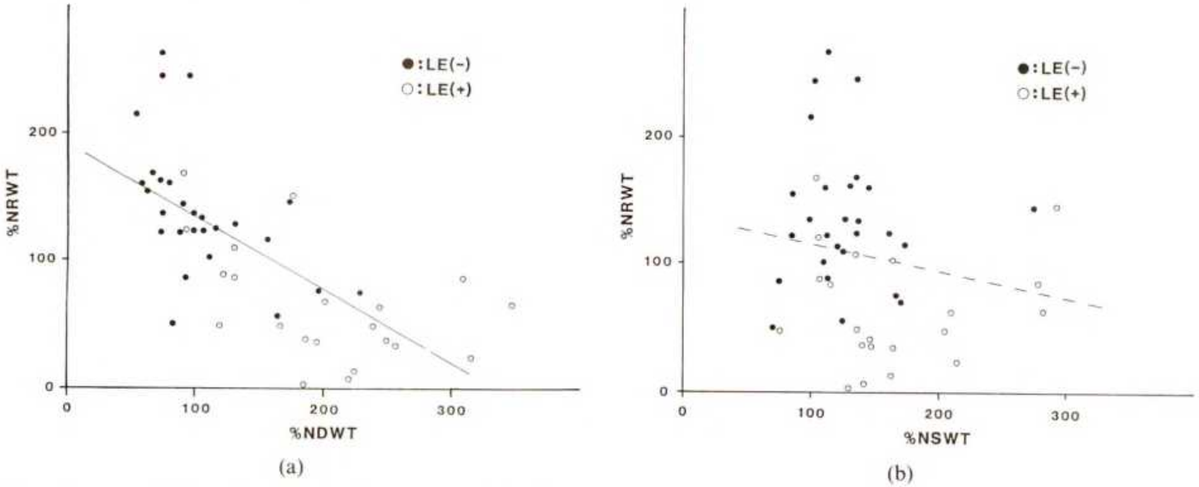
(b)

(c)

Figure 5. Histograms and mean ± SD of (a) the normalized percentage diastolic wall thickness (%NDWT), (b) the normalized percentage systolic wall thickness (%NSWT), and (c) the normalized percentage regional wall thickening (%NRWT) in the segments that showed LE and in those that did not show LE. %NDWT and %NSWT in the segments with LE were significantly larger than those in the segments without LE, $p < 0.001$ and $p < 0.05$. %NRWT in the segments with LE was significantly less than that in the segments without LE, $p < 0.001$.

III). The %NRWT in the segments with LE was significantly less than that in the segments without LE [63.6 ± 44.5% and 137.6 ± 54.6%, respectively; $p < 0.001$; Fig. 5(c)].

The %NRWT had good negative correlation with the %NDWT [$(\%\text{NRWT}) = -0.56 \times (\%\text{NDWT}) + 187.9$; correlation coefficient −0.675; Fig. 6(a)], and had no correlation with the %NSWT [$(\%\text{NRWT}) = -0.21$



(a)

(b)

Figure 6. Relation between (a) the percentage normalized regional wall thickening (%NRWT) and the percentage normalized diastolic wall thickness (%NDWT) and (b) %NRWT and the normalized percentage systolic wall thickness (%NSWT). Open circles are the segments with LE and solid circles are the segments without LE.

× (%NSWT) + 136.2; correlation coefficient −0.186; Fig. 6(b)].

The intraobserver variability for the measurement of the LV myocardial thickness was assessed by measuring the myocardial thickness of controls on two different days. The percentage difference of each myocardial thickness was calculated from the difference of that determination and the average of the two myocardial thickness measurements. The intraobserver variability, calculated as the mean ± SD of percentage differences, was 1.5 ± 1.2%. The interobserver variability assessed by measuring the myocardial thickeness controls was 2.1 ± 2.3%.

The intra- and interobserver variability for the measurement of the LV myocardial CT value were 5.5 ± 7.2 and 5.0 ± 8.5.

Discussion

Our results clearly showed that LE of the LV wall after an injection of contrast medium was related to an abnormal change between minimum and maximum wall thickness of the LV, and with hypertrophy of the LV wall in the patients with HCM.

It is known from dog experiments that ED and LE in cardiac CT indicates myocardial infarction. In old myocardial infarction, LE is thought to correspond to fibrotic scarring with abundant capillaries (Carlsson et al, 1983). These findings have not been used in clinical practice with conventional CT scanners because of poor image quality and poor ability to repeat rapid scanning in cardiac CT examinations. However, the rapid repetition capability of UFCT enables us to use LE and ED in clinical cardiac CT practice (Naito et al, 1990b).

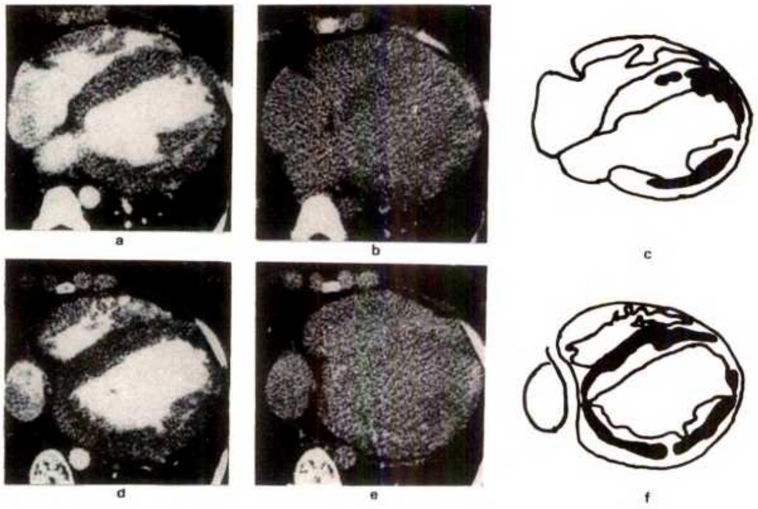


Figure 7. 14-year-old girl. Clinical diagnosis of "dilated" phase of hypertrophic cardiomyopathy. (a, d) Early phase images; (b, e) delayed phase images of the same levels as (a) and (d), respectively. (c, f) Diagrams of late enhancement. Late enhancement was found as diffuse lesions in LV myocardium.

Late enhancement especially was quite sensitive for myocardial infarction. There was, however, no quantitative definition of LE. Our recent study showed that the percentage rise of the myocardial CT value (%RMCT) in normal, severely ischaemic and infarcted myocardium were 54%, 54% and 95% (Naito et al, 1990a). Therefore, in this study we defined the area of LE as the LV myocardial area where %RMCT was over 80%.

Late enhancement, also found in patients with HCM, seemed to correspond with abnormal myocardium. However, there was little evidence of any relationship between LE and different myocardial architecture in patients with HCM.

Left ventricular myocardial lesions, such as myocardial hypertrophy, myocardial disarray and fibrosis, affected regional LV contractile dynamics in patients with HCM (Usuki et al, 1989). Late enhancement was not found as patchy but as diffuse lesions in LV myocardium in two other HCM cases which represented clinically a "dilated" phase (Fig. 7) (Yutani et al, 1985). Myocardial disarray and interstitial fibrosis were marked on the RV biopsy specimens of these patients and another HCM patient, in whom LE was found on the RV endocardial border of the interventricular septum.

We speculate that LE of the LV wall after an injection of contrast medium might be related to different myocardial architecture in patients with HCM. This preliminary study did not show an association between histological abnormality and late enhancement.

We used "the near short-axis position" rather than the exact short-axis position, because our scanner had been installed in such a way that the table tip could not be used.

We used normalized percentage wall thickening, normalized percentage diastolic thickness and normalized percentage wall thickness in this preliminary study. A significant difference between wall thickening in the septum and that in the posterior wall of the LV in normal controls has been reported (Ten Cate et al, 1977; Corya et al, 1977; Usuki et al, 1989), and because of this we believe that normalized parameters should be applied in our analysis.

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Quantitative computed tomography: comparative study using different scanners with two calibration phantoms

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Abstract. To assess computed tomography (CT) scanners in vertebral quantitative computed tomography (QCT) measurement, five cadaveric vertebrae fixed in a water phantom were measured using 16 CT scanners of 10 different models using two types ($CaCO_3$ and K_2HPO_4) of reference phantom. Although the same reference phantoms were used, the QCT values varied markedly depending on the CT scanner employed. The differences in QCT values were greater in the equivalent amount of $CaCO_3$ than in that of K_2HPO_4. The largest difference between CT scanners was 40 mg/cm^3 in the equivalent amount of $CaCO_3$ and 28 mg/cm^3 in that of K_2HPO_4. These differences were reflected among CT scanners by different slopes and intercepts of the reference lines of $CaCO_3$, K_2HPO_4 and ash density depending on the CT scanner used. However, good correlations ($r > 0.97$) were observed for the QCT values obtained by various CT scanners. These results show that QCT values on one machine can be compared more closely with those of another machine if conversion formulae, determined by using materials equivalent to human vertebral bone, are employed.

Osteoporosis is a major public health problem in many countries. Bone strength is mostly dependent on bone mineral content and therefore the measurement of bone mineral content is important to predict osteoporosis-related fractures.

Computed tomography (CT) has been widely used in the measurement of bone mineral density since this method was first employed in 1976 (Rüegsegger et al, 1976) and still has several advantages over other recently developed techniques for assessment of bone mineral content such as dual energy X-ray absorptiometry (DEXA). Only CT can assess bone densities (g/cm^3) in a strict sense and measure cancellous bone alone. However, there are several problems in CT bone mineral measurement, especially in comparing values between different CT scanners. The CT numbers alone are not useful for comparison since these are so variable when obtained under different conditions (Levi et al, 1982) or by different CT scanners (Cann, 1987). Thus, quantitative computed tomography (QCT) using mineral reference phantoms for simultaneous calibration has been widely used in recent years to eliminate this drawback (Cann & Genant, 1980; Genant et al, 1982; Firooznia et al, 1984; Banks & Stevenson, 1986). However, the differing methods of producing CT in different scanners leads to differences in QCT values even with the use of a standardized calibration method (Cann, 1988).

In this study, QCT values of human vertebrae obtained by different types of CT scanner using two different types of calibrating phantom were compared.

Materials and methods

Bone specimen and reference phantom

Vertebral bodies from cadavers were cleaned of surrounding tissue, fixed in 10% formalin solution and washed completely in water. Some ($n = 5$) were used to examine differences in QCT values between various CT scanners and were fixed in the centre of an acrylic water phantom (Fig. 1). Other vertebral bodies ($n = 10$) were used for ash weight correlation.

Two types of reference standard material were used. (1) A solid $CaCO_3$ phantom (B-MAS™: Kyoto Kagaku, Hyouhon Co. Ltd, Kyoto, Japan) is crescent-shaped and consists of urethane resin material of 30 cm in length, 30 cm in width and 3 cm in thickness containing five different cylindrical rods (diameter 1.5 cm) composed of 32.31, 80.17, 133.47, 177.03 and 226.66 mg $CaCO_3$/cm^3, respectively (Fig. 1). Homogeneity of the material was determined and shown to be within 0.1% of variation along the 30 cm long rod. (2) A K_2HPO_4 calibration phantom was composed of five acrylic cylindrical vessels (diameter 1.2 cm) containing aqueous solutions of five different concentrations (0, 50, 100, 150 and 200 mg/cm^3) of K_2HPO_4 and fixed in the bottom of an acrylic water phantom (Fig. 1).

QCT procedure

The acrylic water phantom, in which human vertebrae and K_2HPO_4 standards were fixed, was placed on

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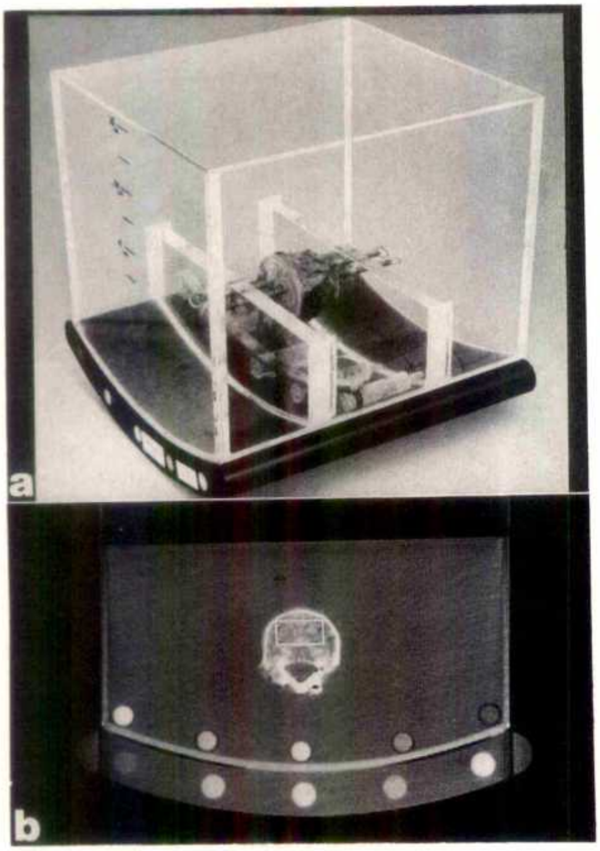

Figure 1. (a) Photograph of an acrylic water phantom used to fix an extracted vertebra on a $CaCO_3$ calibration phantom. (b) CT image of a 10-mm thick section of vertebra, scanned in a water phantom. A rectangular ROI centred in purely trabecular bone is used to obtain the QCT value in relation to calibration standards measured in circular ROIs.

top of the solid $CaCO_3$ phantom and centred in the scan field. Using a lateral computed radiograph for localization, the central section of the vertebral body was scanned simultaneously with both mineral reference phantoms ($CaCO_3$, K_2HPO_4).

When one mineral reference phantom was scanned without another phantom, reference lines were essentially similar to those obtained by placing one phantom over another. Moreover, by comparison with the QCT values of vertebrae obtained using one phantom, potential variation in the QCT values of vertebrae generated with close proximity of the two phantoms were less than 3 mg $CaCO_3/cm^3$ and 2 mg K_2HPO_4/cm^3, respectively. $CaCO_3$ and K_2HPO_4 phantoms were positioned in the same scan image to reduce the measurement errors.

We used 16 CT scanners of 10 different models manufactured by four different companies (Yokogawa/General Electric, Toshiba, Shimadzu and Hitachi/Philips). All QCT scans and calculations were performed by one individual to reduce person-to-person variations. Scans were performed at 120 kVp with a slice thickness of 10 mm on all CT scanners, using mAs suitable for spinal imaging. Regions of interest (ROI) were established in the same location and of the same size (rectangular) but as large as possible, so that the entrance notch of the basivertebral vein and vertebral cortical bone were excluded (Fig. 1).

From the concentrations of each standard substance in the reference phantom and the respective mean CT numbers, the regression equation (regression line) was obtained. The equivalent amounts of $CaCO_3$ and K_2HPO_4 within the trabecular bone region were calculated on the basis of the mean CT number within the rectangular ROI of the human vertebra.

These QCT measurements, when properly performed, showed less than 1.1% coefficient of variation (CV).

Measurement of ash weight of bone specimen

Ten bone samples were excised from 10 human vertebrae corresponding to the scanned volume, for which the mineral density had been previously measured by the QCT method on a Yokogawa/GE CT8600. To ensure that the portion of the vertebrae scanned corresponded to the bone sample, radiographs were obtained to determine the midplanes of each vertebral body and each sample was milled to a slice 10 mm thick symmetrically around the midplane. The ROI size was then measured on the CT image and the same ROI size bone sample was milled from the vertebral body. The precise volumes of the samples were measured using a precision micrometer. They were ashed at 680°C for 20 h in an electric furnace and weighed. From the ash of each of these 10 vertebrae and respective mean CT numbers obtained by QCT measurement, regression parameters were calculated.

Correlations among CT scanners

The mean QCT values obtained by performing five scans with each of 16 CT scanners were compared, and QCT values obtained by 15 CT scanners were also compared with those obtained by one other CT scanner (Yokogawa/GE CT8600).

Reference lines calculated from the concentrations of standard materials ($CaCO_3$, K_2HPO_4 and bone) and their respective CT numbers were also compared on one scanner (Yokogawa/GE CT8600).

Results

A good linear relationship between the concentrations of $CaCO_3$ standard materials and respective mean CT numbers was confirmed, except those of the lowest (32.31 mg $CaCO_3/cm^3$) and highest (223.26 mg $CaCO_3/cm^3$) standard rods on 16 CT scanners. The reason for this non-linearity remains unclear in spite of several possible explanations. The degree of deviation from the linear relationship differed between CT scanners employed (Fig. 2), showing similar tendencies in similar models manufactured by the same company. In our experiments, when the solid $CaCO_3$ phantom was used, the reference lines were obtained from the inter-

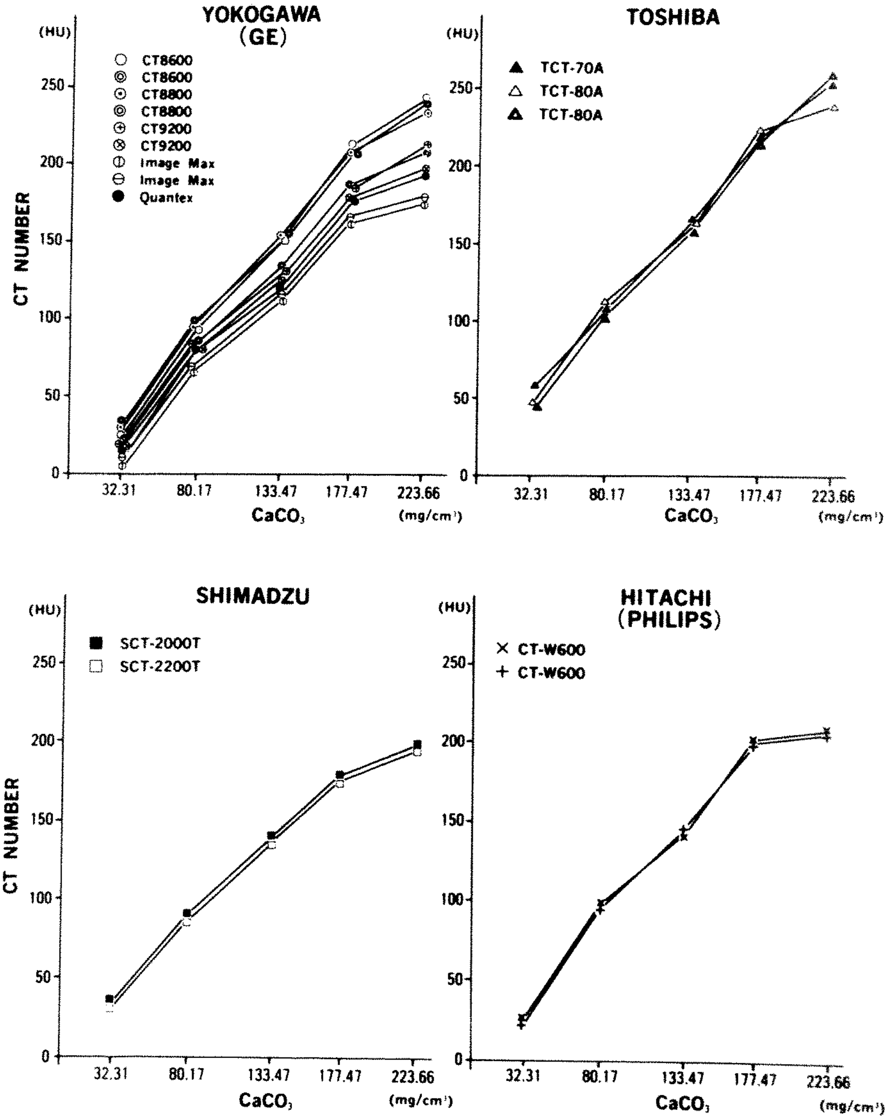

Figure 2. $CaCO_3$ reference lines obtained using 16 CT scanners of 10 different models.

vening three $CaCO_3$ equivalent rods in order to minimize artefacts.

In contrast, when K_2HPO_4 was used as the standard material, the relationship between the concentrations of standard materials and their CT numbers was essentially linear and statistical variations of the regression lines (mineral reference lines) were less than those of the $CaCO_3$ phantom, regardless of the model of CT scanners (Fig. 3).

The reference lines of $CaCO_3$ and K_2HPO_4 showed different slopes and intercepts when different CT scanners were used. In addition, the reference lines obtained from the 10 ash densities and respective CT numbers were different from those of $CaCO_3$ and K_2HPO_4, measured using a single CT scanner (Yokogawa/GE CT8600). The reference line of ash densities was closer to that of K_2HPO_4 than that of $CaCO_3$ (Fig. 4).

The QCT measurement of five extracted cadaver vertebrae, using the solid $CaCO_3$ phantom with 16 CT scanners, resulted in marked differences in the equivalent amounts of $CaCO_3$ by as much as 40 mg $CaCO_3/cm^3$. Fewer differences were observed in the equivalent amounts of K_2HPO_4, using the K_2HPO_4 phantom; the largest difference was 28 mg K_2HPO_4/cm^3.

However, when the QCT values (either equivalent amounts of $CaCO_3$ or K_2HPO_4) of five vertebrae measured with the 15 CT scanners were compared with those obtained with a Yokogawa CT8600 scanner, high correlations ($r > 0.97$, $p < 0.01$) were observed. Variations in the slopes and intercepts of the regression

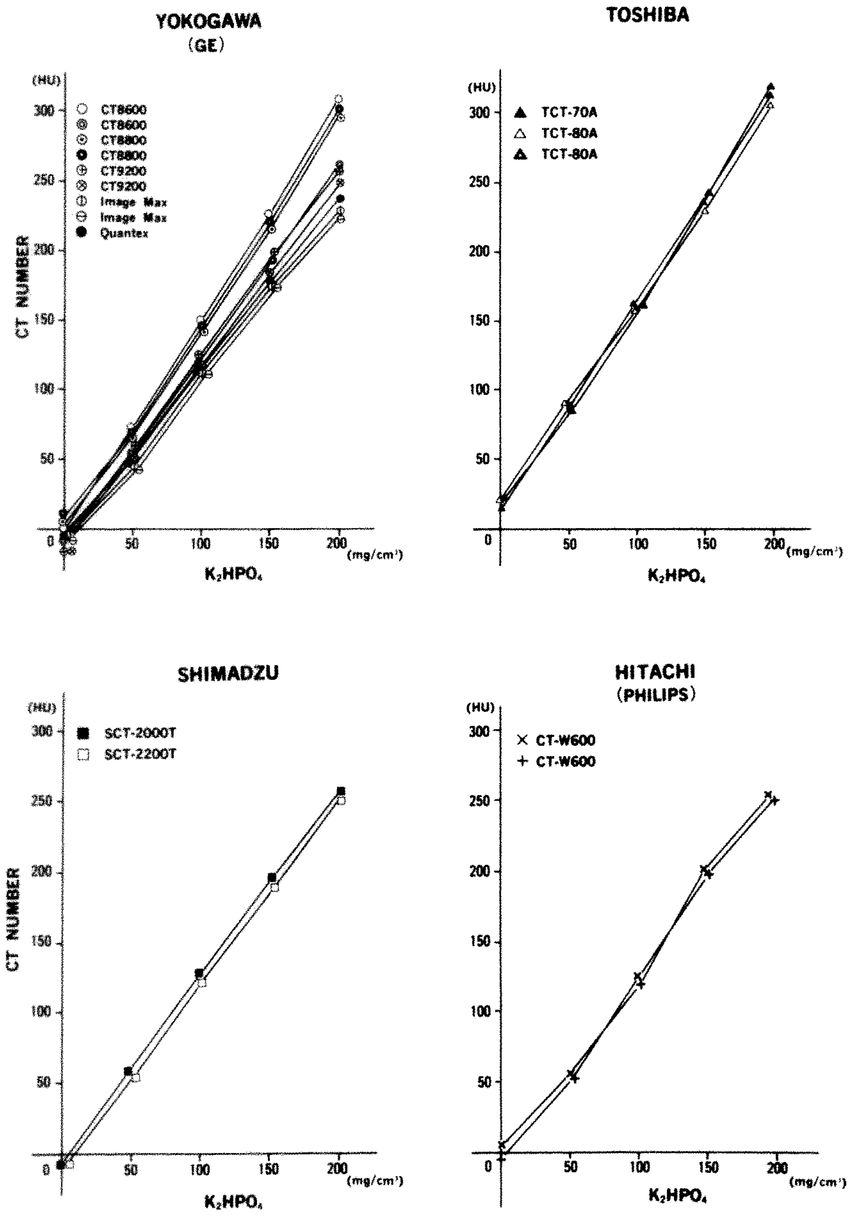

Figure 3. K_2HPO_4 reference lines obtained using 16 CT scanners of 10 different models.

lines of the QCT value correlationship were less when using the equivalents of K_2HPO_4 than of $CaCO_3$ (Table I). Furthermore, each CT scanner had its own particular tendency either to overestimate or underestimate QCT values.

Discussion

QCT values of trabecular bone regions of the lumbar vertebrae have been used for the diagnosis of osteoporosis and the determination of spinal compression fracture thresholds (Cann et al, 1985; Firooznia et al, 1986). A consensus for QCT values of fracture thresholds would be useful. However, our study shows that these values obtained by one institution are not directly applicable to other institutions with a different scanner (Genant et al, 1985; Firooznia et al, 1986; Cann, 1987).

The lines relating $CaCO_3$, K_2HPO_4 and cadaver vertebrae (ash density) and CT numbers had different slopes and intercepts, depending on the CT scanner used. In our study, since the line relating ash densities and their CT numbers is close to that of K_2HPO_4, the differences between QCT values would be smaller when expressed as equivalent amounts of K_2HPO_4 rather than of $CaCO_3$, and can be attributed to a closer X-ray attenua-

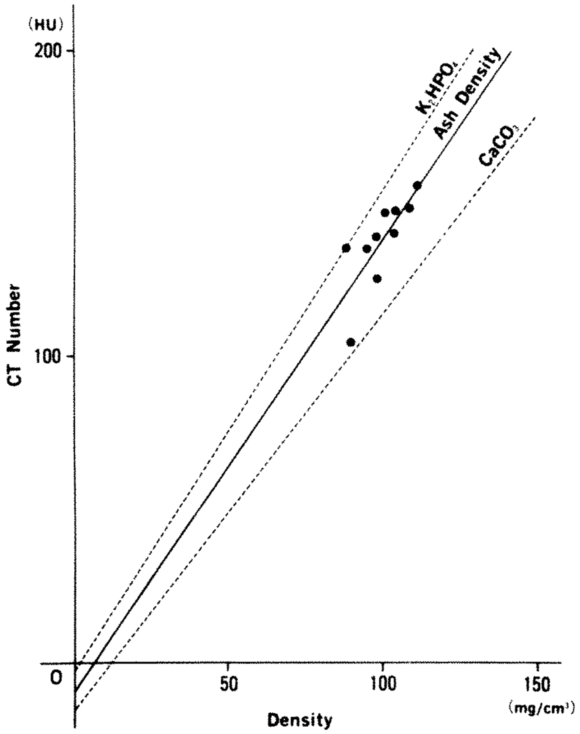

Figure 4. Relationship between CT number and ash amount in 10 vertebral bodies. A Yokogawa CT 8600 scanner was used in the assessment. The best-fit regression line is given by CT No. = 1.46 Ash − 8.7 with a standard error of the estimate (SEE) of 9.8 mg/cm^3 and a correlation of 0.77 ($p < 0.01$). Reference lines of $CaCO_3$ and K_2HPO_4 obtained with the Yokogawa CT8600 scanner are also added.

tion of bone mineral to K_2HPO_4 solution than to $CaCO_3$ rods.

Different slopes and intercepts of the lines are attributable to changes from delayed correction of CT numbers, variations in the sensitivity of detectors in CT scanners, kinds of software that convert absorption coefficients into CT numbers, etc. (Cann, 1988). A mineral reference phantom using calcium hydroxyapatite as a standard material was recently produced (Adams & Adams, 1987; Kalender & Suess, 1987; Richmond et al, 1987). These new solid phantoms using hydroxyapatite might be more suitable for reducing machine-to-machine variations than the $CaCO_3$ phantom. The correlations of calcium hydroxyapatite are presumably close to that of genuine trabecular mineral (bone ash), but not entirely the same. Therefore, differences between QCT values obtained using various CT scanners and this reference would remain to be evaluated.

Another problem is the presence of marrow fat, which can modify the QCT values of vertebrae on single-energy QCT measurement. The relation in Fig. 4 between CT attenuation and ash is linear and significant, but is not of a high order. A dual-energy QCT measurement would be needed to reduce this fat effect. However, because there were good correlations between QCT values in different machines, as shown in Table I, the influence of marrow fat was negligible on comparison of QCT values between CT scanners. A reference material similar to vertebral bone (including marrow fat) would be theoretically necessary for single-energy QCT measurement to minimize institution-to-institution variations.

The differences between QCT values using various CT

Table I. Correlation between the QCT values by the Yokogawa CT8600 scanner and those by other 15 CT scanners

CT scanner		$CaCO_3$		K_2HPO_4	
Manufacturer	Model	Slope	Intercept	Slope	Intercept
Yokogawa (General Electric)	CT8600	1.03	−6.98	1.10	−4.80
	CT8800	1.04	−10.77	1.10	−8.85
	CT8800	1.06	−14.74	1.09	−9.98
	CT9200	1.05	−7.71	1.18	−12.02
	CT9200	0.94	2.16	1.05	−2.48
	Image Max	1.06	0.60	1.24	−11.91
	Image Max	0.94	6.07	1.09	−4.03
	Quantex	0.87	3.43	1.02	−2.79
Toshiba	TCT-70A	1.04	−11.57	1.01	−3.12
	TCT-80A	1.01	−12.19	1.05	−8.68
	TCT-80A	1.11	−29.37	1.09	−21.03
Schimadzu	SCT-2000T	1.11	−18.82	1.11	−4.70
	SCT-2200T	1.08	−12.91	1.11	−2.31
Hitachi (Philips)	CT-W600	0.85	−7.63	1.01	−10.99
	CT-W600	0.86	−7.00	0.99	−8.32
Mean		1.00	−8.50	1.08	−7.73
Standard deviation		0.09	8.89	0.06	4.93

Note: Regression parameters against values for the Yokogawa CT8600 scanner are listed for each CT scanner.

scanners are not negligible (maximum: 40 mg $CaCO_3/cm^3$, 28 mg K_2HPO_4/cm^3). To reduce this discrepancy in QCT values using different CT scanners, manufacturers would need to improve their algorithms and software. Besides this, comparison of the QCT values between different CT scanners should be possible, since good correlations were observed between QCT values irrespective of the CT scanner employed. K_2HPO_4 reference curves (Cann, 1987) cannot be used for comparison of QCT values from different CT scanners. Our results show that QCT values on one machine could be compared more closely with those of another machine by conversion formulae, determined using materials equivalent to human vertebral bone.

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Initial investigation of childhood urinary tract infection: does the plain abdominal X ray still have a role?

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Abstract. To reassess the plain abdominal X ray (AXR) in the initial investigation of childhood urinary tract infection, radiologists from four paediatric units prospectively collected data on the yield from the AXR in 683 children. Five children had renal calculi. All were detected on ultrasound, but one was not visible on the initial AXR. Four spinal abnormalities were identified, none of which prompted any action by the clinician involved. While the costs, in both financial and radiation risk terms, may be small, the benefit of the AXR appears equally small. Where expert paediatric ultrasonography is available we would recommend that the AXR be reserved for patients with haematuria, loin pain, family history of calculus disease, or where further urinary tract infection occurs despite a normal ultrasound scan.

The place of the plain abdominal X ray (AXR) in the initial investigation of childhood urinary tract infection (UTI) has remained unchallenged since its introduction. Until the early 1980s the intravenous urogram (IVU) was the usual first investigation of a UTI with or without a voiding cystourethrogram. The AXR was performed as the control radiograph of the IVU. As most paediatric units replaced the IVU with ultrasound (US), the AXR was retained to detect radio-opaque calculi that the US might miss, or spinal anomalies that might be the cause of abnormal bladder function. This approach would seem logical, but we have been unable to find any hard evidence of its necessity. We present a four centre study designed to address the question: Given the current availability of high quality US apparatus and trained paediatric operators, does the AXR still have a role in the initial investigation of first hospital presentation of childhood UTI?

Methods

Paediatric radiologists from Belfast, Brighton, Edinburgh and Leeds agreed to participate in the study. All children referred for initial investigation of UTI between June 1988 and December 1989 were considered eligible. Although it is the general policy of all participating units not to investigate unproven UTIs, we felt that to insist on laboratory confirmation of pure culture growth at 10^5 organisms/ml was unnecessarily rigid and therefore accepted our routine referral population as representing the real situation in which the lessons learned from this study would be applied. As far as was practical the cases were consecutive and were scanned under the direction of experienced paediatric radiologists.

The US was performed and interpreted before viewing the AXR. A record was kept of calculi or calcification on either study, and of any spinal abnormality considered significant. The presence of spina bifida occulta was not recorded.

Results

A total of 683 patients were included in the study. The age distribution ranged from 1 month to 13 years, being concentrated primarily in the first years of life with 59% below the age of 5 years. Renal calculi were present in five cases, all of which were detected during the US study, but in one case the calculus was not visible on the AXR. This small right renal calculus was later proven on the preliminary radiograph of an IVU, which was otherwise normal. The case details are recorded in Table I. One case of nephrocalcinosis was demonstrated on both US and AXR.

Four spinal abnormalities were noted. Two were lumbar scolioses, one of which was already known to the orthopaedic surgeons; the other was ignored by the clinical staff and therefore cannot be considered relevant. A child already considered to have the Vater syndrome had a minor sacral anomaly, while another child had the incidental finding of an L5 spondylolysis. This was asymptomatic and was not acted on by the clinicians.

Discussion

Since US replaced the IVU as the initial screening method in the first hospital presentation of childhood UTI, the AXR has been regarded as essential to detect

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Table I. Details of cases with renal calculi

Age (years)	Sex	Presentation	Family history	Urine culture	AXR	US
3	M	Recurrent UTIs Haematuria	None	Proteus	Left staghorn	Left renal calculus
2	M	UTI Haematuria	Sibling and father	Coliforms	Multiple right calculi	Multiple right renal calculi
3	M	UTI Dysuria Haematuria	None	*E. coli*	Normal[a]	Right renal calculus
3	M	UTI Haematuria	None	Sterile[b]	Left renal calculi Right staghorn	Bilateral calculi
7	F	UTI No haematuria	None	Coliforms	Right renal calculi	Right renal calculi

[a] Stone later confirmed on the control radiograph of an intravenous urogram.

[b] General practitioner referred case as proven UTI, but specimen at clinic was sterile.

renal calculi and spinal anomalies (Whitaker & Sherwood, 1984; Gordon, 1987).

Where there is high quality ultrasound equipment, and more importantly, paediatric radiologists and sonographers to use it, is the AXR still justified? This question begs the answers to several others:

—In how many instances does the AXR reveal an abnormality that affects management?
—What would be the clinical consequence of missing these abnormalities during initial screening?
—What would be the benefits of omitting the AXR?

The yield of the AXR

We are not aware of any previous data relating directly to the yield of the AXR in childhood UTI. Urinary tract calculi are uncommon in children. Over 23 years 113 children had surgical procedures for calculi at the Royal Hospital for Sick Children in Glasgow (MacDonald & Azmy, 1988), of which only 50 had proven UTI. At Great Ormond Street Hospital, London, a tertiary referral centre, 95 of 120 cases of urinary calculi had infected urine (Ghazali et al, 1973). In our case material, the incidence of renal calculi was five out of 683 or 0.7%; all calculi were seen on US whereas one was not visible on the AXR.

To the best of our knowledge, details of the detection of spinal abnormalities by AXR in this clinical situation have similarly not been reported. It is not the current policy of the radiologists participating in this study to comment on spina bifida occulta for the following reasons. (1) It has, to date, not resulted in any clinical action. (2) Non-fusion of the posterior laminae is normal in early childhood. (3) The presence or absence of a defect may be very difficult to ascertain on an AXR owing to overlying bowel shadows. (4) Spina bifida occulta is extremely common and in isolation is not considered a significant finding (Fawcitt, 1958). A large random sample of 2707 healthy adults found a 23% incidence of spina bifida occulta but no other spinal anomalies (Fidas et al, 1987). Our incidence of spinal abnormalities, spina bifida occulta excluded, was four out of 683 or 0.6%. In only two cases was the diagnosis not already known or suspected. One child had a hemivertebra at L3/4 with a mild scoliosis, while another had a spondylolysis at L5. In neither case were there signs or symptoms and no follow-up or action was taken by the clinicians.

Out of 683 AXRs, therefore, not one could be said to have produced any additional positive benefit to the child.

Potential risks of omitting the AXR

In retrospect all 683 children could have had the AXR omitted with no significant consequences. However, if the AXR is omitted from the screening investigation of UTI, inevitably a small number of abnormalities will initially go undetected. The risk for both calculi and spinal problems is that a further UTI results in irreversible renal damage. The degree of risk is not known, but assuming the UTI causing referral has been effectively treated and it is understood that a further UTI requires prompt treatment and further investigation, it should be small. We would not propose to abandon the AXR altogether but rather to use it in a selected group initially, and as a routine procedure in all children in whom initial screening is negative but a further UTI occurs. Prompt treatment of UTI is vital in limiting the risk of renal damage. In first presentation of UTI, restriction of the AXR to those children with loin pain, haematuria, family history of stone disease, neurological problems or abnormal micturition would cut the number of screening radiographs by 70–80%. An AXR would be part of the routine investigation of a second UTI where initial US was negative.

Benefits of omitting the AXR

These can be considered in terms of cost and radiation savings. Gauging the true cost of radiographic studies is difficult while the capital value of buildings and equipment is still being assessed. Data from the Whittington Hospital (Bretland, 1988) suggests that £20 would be a reasonable estimate for the performance of a plain radiographic study. Using this figure gives a cost for 683 AXRs of £13,600 for no significant gain.

The estimation of radiation risk is similarly difficult. Using the International Commission on Radiation Protection (ICRP) estimate, which is an average for age and sex, the rate of induction of fatal cancers is 125 deaths per million people per 10 mSv. The mean absorbed dose equivalent for the AXR in adults is in the region of 1.4 mSv (Shrimpton & Wall, 1986). In the absence of good data for pre-school children we have calculated the mean absorbed dose equivalent of 0.36 mSv for a 1–2 year old, based on an average measured skin dose of 0.8 mSv, assessment of the organs included in the X-ray beam, their depths and relative sensitivity. This gives an estimate of fatal cancer risk in our study of $(125)\times(0.36/10)\times(683/1\,000\,000)$, or 0.0031. In other words there is a probability of inducing one fatal cancer for every 220 000 AXRs (683/0.0031). We stress that this is based on considerable uncertainty, but may underestimate the risk in childhood (Bross & Natarajan, 1972; Sumner, 1988). Considering the additional risks of non-fatal malignancy and genetic consequences, the risk of performing the AXR, although small, cannot be completely disregarded. As recently stressed by a joint report from the Royal College of Radiologists and the National Radiation Protection Board (NRPB, 1990), the single largest reduction of patient radiation dose is by the elimination of unhelpful examinations.

Conclusion

The use of the AXR in initial investigation of UTI has an extremely low yield and a significant financial cost. Considering the numbers involved and the lack of proven benefit, what may seem a small radiation dose penalty may be considered unwarranted. We suggest that where the ultrasound is performed by experienced paediatric staff, the AXR is abandoned as a routine procedure and used where positively indicated. Where scanning expertise is less specialized, the AXR may still have an important role.

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Floating thrombi: diagnosis and follow-up by duplex ultrasound

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Abstract. The clinical features and evolution of floating thrombi (FT) diagnosed by duplex ultrasound were examined. In 76 consecutively diagnosed above-knee deep venous thromboses the prevalence of FT was 18%. Of 44 FT diagnosed in 39 patients, 18 (39%) were located in the common femoral, 12 (26%) in the popliteal and seven (15%) in the external iliac veins. Serial duplex examinations revealed that 31% of FT in the iliofemoral segment disappeared, 33% remained unchanged and 36% adhered to the vein wall within 2 weeks following diagnosis. After 3 months, 87% of the floating segments had disappeared, irrespective of the localization or therapeutic regimen. Thirteen patients experienced pulmonary embolism before (12/13) or following (4/13) diagnosis of floating thrombosis; three of four superficial femoral vein FT embolized. Fifteen per cent of the patients with FT died during the study period and 28% of the thrombi were associated with a malignant neoplasm; the incidence of malignancy was 60% in superficial and 39% in common femoral vein FT.

The majority of symptomatic pulmonary emboli and most fatal emboli arise from deep venous thrombi in the pelvis and lower extremities (Havig, 1977). For the treatment of deep venous thrombi and prevention of pulmonary emboli, it is important to know whether some thrombi represent an increased risk for embolization and how they can be distinguished.

During the last decade, several authors have emphasized that floating iliofemoral thrombi are a significant risk for pulmonary embolism (Savelyev et al, 1980; Ehringer & Minar, 1987; Akers et al, 1987). Nevertheless, clinical information about floating thrombi (FT) is still scarce. We evaluated retrospectively the prevalence, anatomical distribution, evolution and clinical significance of FT in a series of patients suspected of deep vein thrombosis. All patients were studied with serial duplex examinations, which proved to be both reliable and sensitive for the non-invasive diagnosis of above-knee deep vein thrombosis (Becker et al, 1989; White et al, 1989).

Materials and methods

In patients suspected of deep vein thrombosis, duplex examination was performed on both legs from the popliteal to the iliac veins, according to the technique described by Talbot (1986). Examinations were carried out with a duplex scanner (Ultramark 8, Advanced Technology Laboratories, Bothell, Washington) fitted with a 5, 7.5 and 10 MHz multifrequency transducer. Diagnosis of deep vein thrombosis relied on non-compressibility of the vein, the presence of intraluminal reflections and the absence of normal venous Doppler signals. Compression of the external and common iliac veins could not ordinarily be effected and diagnosis of iliac vein thrombosis relied on the last two criteria, provided that the iliac vein segment could be clearly seen. A thombus was considered to be free-floating if only the distal part adhered to the vein wall, while the proximal segment moved freely in the bloodstream when (gentle) pressure was applied to the calf. Patients were examined in anti-Trendelenburg or 45° recumbent position, which provided good venous dilatation, allowing optimal visualization of the echo-free rim that surrounded the floating segment (Fig. 1). In this rim, Doppler signals could often be detected. Floating thrombi moved to and from the vein wall, but very long thrombi were also observed to move along the long axis of the vein.

The prevalence of above-knee FT was determined in a consecutive series of 216 patients suspected of deep vein thrombosis within a 4-month period (1 January to 1 May, 1989). The anatomical distribution was studied in a 28-month period (1 January 1987 to 1 May 1989). Floating segments were located within the iliac, common femoral, superficial femoral, profunda and popliteal veins or within the proximal part of the long saphenous vein.

The floating segments were evaluated 2 weeks and 3 months after the initial diagnosis for change, complete disappearance and for adherence to the vein wall. Furthermore, the evolution of the floating segment was evaluated both with respect to the therapeutic regimen and the anatomical distribution. Statistical differences between the effects of different therapeutic regimens were computed by χ^2 with Fisher's exact test. To determine the clinical significance of FT, the clinical records of the patients were reviewed.

Patients

Between 1 January 1987 and 1 May 1989, 39 patients (21 male and 18 female; mean age 59 years, range 19–85 years), presented with FT (1987: 8 patients; 1988: 17;

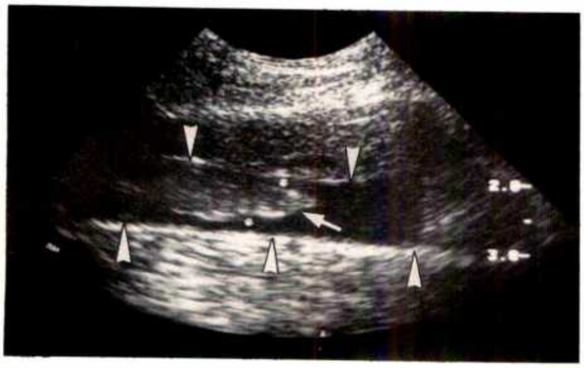

Figure 1. Common femoral vein floating thrombus (arrow) with echo-free rim (*) between the thrombus and the vein wall (arrowheads).

1989: 14). Four patients died at 1, 3, 5 and 22 days, respectively, after diagnosis; two underwent thrombectomy 1 day following duplex examination. Three patients were lost to follow-up. In 30 patients (16 male and 14 female; mean age 59 years, range 19–85 years), the evolution of the thrombus could be evaluated 2 weeks and/or 3 months after diagnosis.

Results

Prevalence

In 76 out of 216 patients (35%) suspected of deep vein thrombosis, a thrombus was demonstrated within or proximal to the popliteal veins; 14 thrombi (18%) met floating criteria. Fifty-one thrombi (67%) were in the iliofemoral segment, of which nine (18%) met floating criteria.

Anatomical distribution

Forty-four FT extending over 46 veins were diagnosed in 39 patients. The localization of the floating segments is shown in Table I. Twenty-four thrombi were located on the right and 20 on the left side.

Evolution

Thirty-five FT extending over 37 veins were followed. The thrombi were located in the external iliac (4), common femoral (14), superficial femoral (4), profunda (1), popliteal (9) and long saphenous (1) veins. Two thrombi extended over both the external iliac and common femoral veins. Eighteen thrombi were on the right and 17 on the left side.

Table I. Anatomical distribution of floating thrombi (46 veins)

	Veins with floating thrombus	
	Number	%
External iliac vein	7	15
Common femoral vein	18	39
Superficial femoral vein	5	11
Profunda vein	1	2
Popliteal vein	12	26
Long saphenous vein	3	7
Total	46	100

Twenty-nine FT in 31 veins were examined 2 weeks after the initial diagnosis. Eleven thrombi had completely disappeared, eight (27%) were unchanged and nine adhered to the wall; one thrombus extending over two venous segments showed complete disappearance of the proximal and adherence of the distal segment. Thus, 40% of the FT disappeared and 33% became adherent to the wall. Considering the 21 FT in the iliofemoral segment, consisting of the external iliac, common and superficial femoral veins, 31% disappeared, 36% became adherent and 33% remained unchanged. The evolution of the floating segments with respect to anatomical distribution is shown in Table II.

Table III summarizes the evolution after 2 weeks of treatment with anticoagulants or with thrombolytic agents followed by anticoagulant therapy.

Three months after diagnosis 27 thrombi extending in 29 veins were examined. Eighty-seven per cent of the floating segments had disappeared and 13% adhered to the vein wall. Twenty-three thrombi completely disappeared, three became adherent and one extending over two venous segments disappeared partially with adherence of the distal segment. Of three floating segments that became adherent to the vein wall, two had totally disappeared 220 and 280 days, respectively, after the initial diagnosis. Twenty-five out of 29 veins (86%) became free of thrombus. The four persisting thombi were in the common femoral vein.

Floating thrombi and pulmonary embolism

In 13 out of 39 patients (33%), pulmonary embolism occurred between 5 days before and 4 days following duplex diagnosis of FT. Diagnosis of pulmonary embolism was confirmed by ventilation–perfusion lung scans in 11 patients (eight scans showed high and three low probability), and by pulmonary angiography and

Table II. Evolution of floating thrombi after 2 weeks, in relation to localization (31 veins)

	Number of thrombi		
	Disappearance	No change	Adherence
External iliac vein	2	3	—
Common femoral vein	3	3	8
Superficial femoral vein	3	1	—
Popliteal vein	4	1	1
Profunda vein	1	—	—
Long saphenous vein	—	—	1
Total	13	8	10

Table III. Effect of anticoagulants and fibrinolytics on floating thrombi 2 weeks after diagnosis (29 thrombi)

		Evolution of thrombi					
		Disappearance		No change		Adherence	
Treatment	Number of thrombi	Number	(%)	Number	(%)	Number	(%)
Anticoagulants	21	6.5^a	(31)	8	(38)	6.5^a	(31)
Fibrinolytics	8	5	(62)	0	(0)	3	(38)
Total	29	11.5	(40)	8	(27)	9.5	(33)

^{a} One thrombus extended over two venous segments, adhering in one and disappearing in the other.

autopsy in one patient each. In 12 patients, pulmonary emboli occurred before diagnosis of FT; the thrombi were located in the external iliac (2), common femoral (3), superficial femoral (1), popliteal (4) and long saphenous (1) veins; one patient presented with a floating thrombus in both the right external iliac and the left common femoral vein.

Four patients experienced massive pulmonary emboli 1 (two patients), 3 and 4 days, respectively, after duplex diagnosis of FT; two of the FT were in a common and two in a superficial femoral vein. Two patients died and two recovered.

Floating thrombi and malignancy

In 28% (11/39) of the patients with FT, a tumour was diagnosed. Malignancy was proved in 10 patients; the histological diagnosis of an intracerebral tumour was not known (Table IV). Except for one patient the presence of cancer was known before the diagnosis of FT. Table IV shows the anatomical distribution of the FT in the patients with tumour. Fourteen per cent of patients with external iliac FT, 39% with common femoral FT, 60% with superficial femoral FT and 25% with popliteal FT presented with a tumour.

Table IV. Tumours in patients with floating thrombi (11 patients)

	Number of tumours	Localization of floating thrombus
Carcinoma of:		
breast	1	CFV
cervix	1	CFV
lung	2	(1)CFV (2)SFV
prostate	1	CFV
rectum	1	PV
Glioblastoma multiforme	1	SFV,PV,CF+EIV
Myelofibrosis with myeloid metaplasia	1	SFV
Polycythaemia vera	1	CFV
Pontocerebellar tumour(?)	1	PV
Primary macroglobulinaemia	1	CFV
Seminoma of the testis	1	CFV

CFV = common femoral vein; CF+EIV = thrombus extending over the common femoral and external iliac vein; SFV = superficial femoral vein; PV = popliteal vein.
? = unknown histological diagnosis.

Mortality

Six patients (15%) died during the study period. Four of them had a malignant tumour: two experienced fatal pulmonary embolism and two died because of generalized metastasis. One patient died because of intestinal haemorrhage due to heparin therapy, and in one patient with an intracerebral tumour the cause of death is not known.

Extension of floating thrombi

Eight patients had venous duplex examination 1–31 days (median 8.5 days) before the diagnosis of FT. Six of them demonstrated a pre-existent occlusive deep vein thrombosis; the floating thrombus developed at the proximal end of the pre-existent thrombus in four patients and in a venous segment distal to it in two patients.

In two patients with FT in a superficial femoral vein, serial duplex examinations showed gradual extension of the floating segment up into the common femoral vein: in one patient thrombectomy was performed; in the other the floating segment, after spontaneous separation from its base, was entrapped in a pre-existent non-occlusive thrombus in the common femoral vein.

Discussion

The radiographic features of FT were first described by Fallenius (1942). Browse reported that up to 47% of deep venous thrombi have a proximal segment non-adherent to the vein wall, which was considered to enhance the risk of embolization (Browse & Thomas, 1974). In our study, 18% of deep venous thrombi in the pelvis and lower extremities met floating criteria and 67% of the FT were located in the iliofemoral segment. The high prevalence of non-adherent thrombi in the study by Browse by comparison with our results suggests that this author included thrombi with an uppermost segment that, although non-adherent, showed no floating movements in the bloodstream. In a study by Norris and colleagues, evaluating the risk of embolization of venographically proven iliofemoral thrombi, only 6% of iliofemoral thrombi met floating criteria (Norris et al, 1985). These authors probably underestimated the prevalence of FT, as the minimal length of the floating segment outlined by radio-opaque contrast medium had to be 5 cm. In our study, using dynamic ultrasound criteria, the length of the thrombus was not considered. However, we assume that we also may have overlooked some small FT so that the real prevalence of FT presumably exceeds 18%.

Two weeks after diagnosis, 31% of FT in the iliofemoral segment had disappeared either by lysis or embolization, 36% became adherent to the vein wall and 33% were unchanged, still moving freely in the bloodstream. Hence 2 weeks after diagnosis, when most patients with deep vein thrombosis are encouraged to resume active mobilization, one out of three patients were still harbouring a floating thrombus. Floating thrombi are generally considered to be an absolute indication for patient immobilization (Ehringer & Minar, 1987). However, controlled studies of the necessity for, and the duration of, the immobilization period are not available. Furthermore, the potential risk of a pulmonary embolus from a floating thrombus older than 2 weeks has still to be determined. In our experience we suggest that complete lysis of FT or adherence to the wall may justify early mobilization; however, persistence or proximal extension of a floating segment should lead the physician to consider more invasive interventional strategies.

In our study the efficacy of different therapeutic regimens could not be compared because of the small number of patients (Table III). In three patients, thrombolytic therapy failed. In one patient, treatment was interrupted prematurely because of major haemorrhage. In another patient a floating thrombus developed within the common femoral vein during thrombolytic treatment of an occlusive iliac vein thrombosis, possibly from stagnating circulation. In a third patient a floating thrombus was at first treated with intravenous heparin; after 4 days a massive pulmonary embolism occurred, which was treated with thrombolytics for only 2 days. Excluding these three patients in whom the effectiveness of lytic therapy can be questioned, the effect of fibrinolytics on FT seems to be superior to that of anticoagulants. These data suggest that FT will disappear more frequently and sooner with fibrinolytic than with anticoagulant therapy ($p < 0.01$). This may be prognostically important, as complete lysis of a floating thrombus eliminates the risk of embolization at least from the floating segment. However, disappearance of FT may also be due to embolization; indeed even fatal pulmonary emboli have been reported during lytic therapy (Ott et al, 1986; Meissner et al, 1987).

Three months after diagnosis, 87% of FT, and 6 months later up to 94% of FT, had disappeared, irrespective of the therapeutic regimen. These data are in agreement with previous studies showing complete recanalization of thrombosed veins in the vast majority of patients with deep vein thrombosis, at long-term follow-up (Huisman et al, 1988; Killewich et al, 1989).

The prevalence of symptomatic pulmonary emboli occurring after duplex sonographic diagnosis of FT was 9% (4/44) if all and 14% if only the 28 iliofemoral FT were considered. This is much lower than the 60% reported by Norris et al (1985). As in the study by Norris et al, all our patients were receiving therapeutic heparinization when the pulmonary embolus occurred.

Four patients experienced massive pulmonary embolism following diagnosis of floating thrombosis. Two pulmonary emboli originated from thrombi within the common femoral vein. The two floating segments that embolized could not be distinguished by duplex criteria from the 15 that did not. Two pulmonary emboli originated from the superficial femoral vein. The floating segment of both thrombi was more than 10 cm long and moved several millimetres along the long axis of the vein on calf compression. A third thrombus with the same characteristics also detached from the vein wall but was entrapped by a pre-existent non-occlusive thrombus in the common femoral vein. A fourth thrombus was surgically removed after it extended up into the common femoral vein. A fifth small floating thrombus did not embolize. From these data, a floating thrombus more than 10 cm long in the superficial femoral vein seems to be very prone to embolize.

Thirty-three per cent of the patients with FT experienced pulmonary emboli. None of 13 patients with FT either in the popliteal vein (nine patients) or external iliac vein (four patients) experienced a symptomatic pulmonary embolism in the follow-up period. These findings would suggest a low risk of embolization of these thrombi. However, in 12 out of 13 patients with the diagnosis of FT after the embolic event, four showed a floating thrombus in a popliteal vein and three in an external iliac vein. Thus, the risk of pulmonary embolism in popliteal or iliac vein FT still needs to be evaluated in larger series.

Finally, we are not aware of objective data comparing the prevalence of pulmonary emboli from floating and from non-floating thrombi.

The association of a malignant neoplasm and thrombosis is well known (Bell et al, 1985). It is not limited to occlusive adherent thrombi as was demonstrated in our study. The incidence of (malignant) neoplasm in patients with FT was 25%: it was 39% in patients with a common femoral vein thrombosis and 60% in patients with a superficial femoral vein thrombosis. In two out of three of the patients with the histological diagnosis of a malignant tumour and a floating thrombus, the thrombus was present in the common femoral vein. This is in contradistinction to the study by Cohen who found the majority of FT within the superficial femoral vein in cases of malignancy (Cohen et al, 1988).

The 15% mortality rate during our study period illustrates the bad prognosis of FT, and is in agreement with the study by Widmer et al (1985) who observed

16% mortality 5 years after unilateral deep vein thrombosis. Five out of six patients who died had a neoplasm and half of the patients with histologically proven malignancy died within 1 month following duplex diagnosis of the floating thrombus. Our series is too small to compare the causes of death with the findings of Widmer et al.

Our study also illustrates that new thrombi can appear and pre-existent thrombi can grow despite heparinization or fibrinolysis. These findings indicate the need for close control of both adherent and non-adherent thrombi, especially during the first 2 weeks following diagnosis. A non-invasive and sensitive technique such as duplex ultrasound seems to be very suitable for this purpose.

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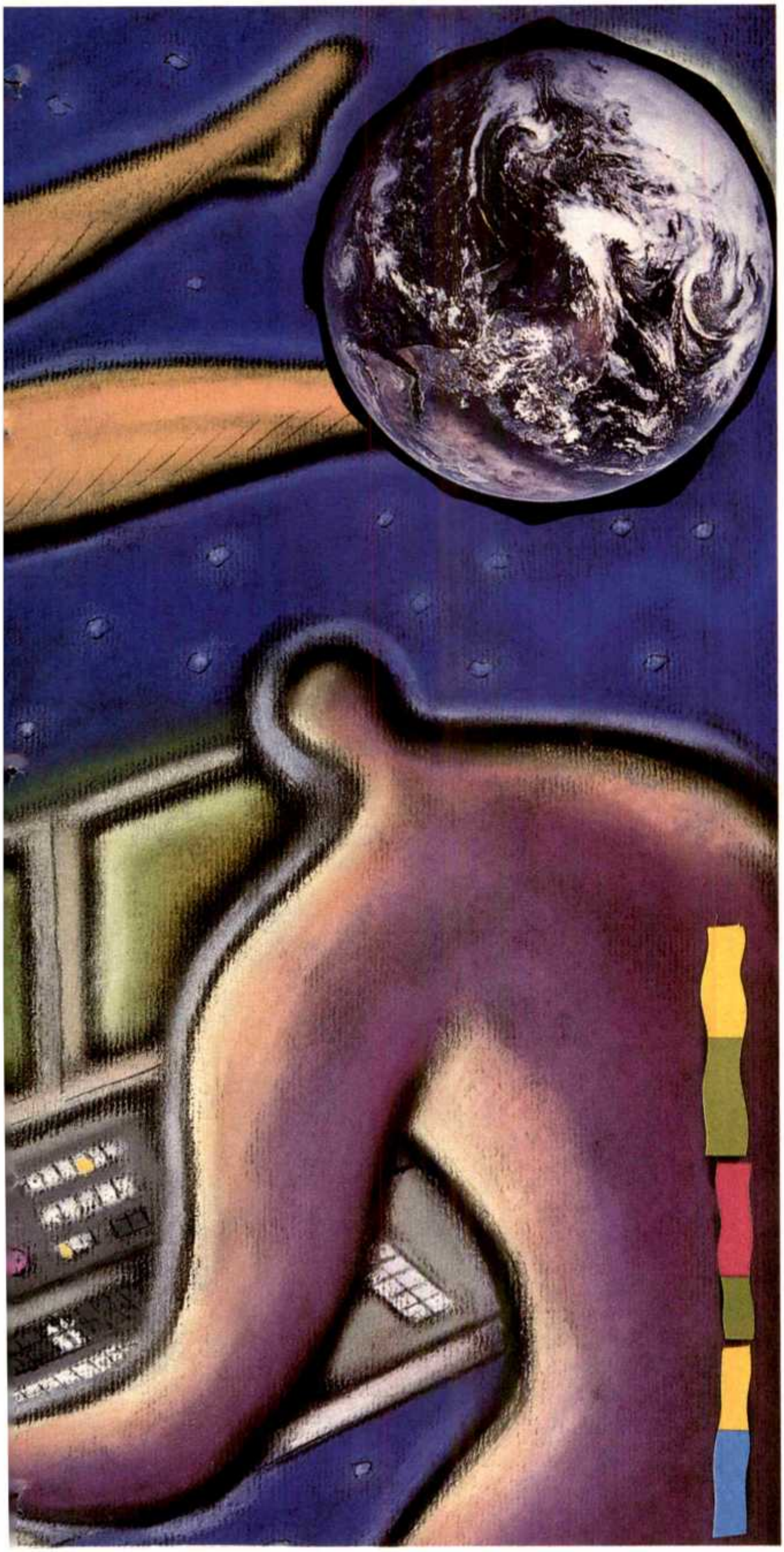

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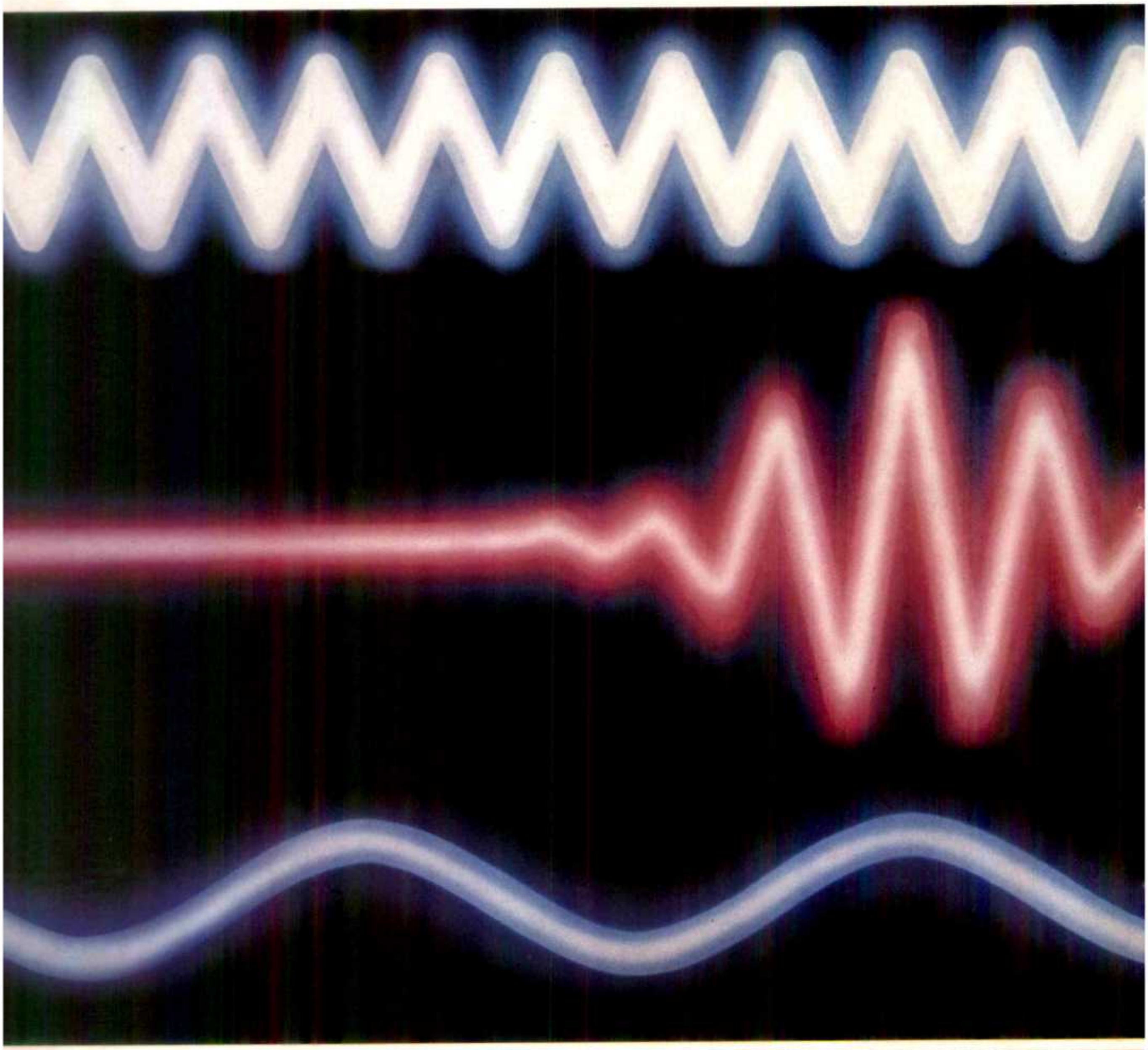

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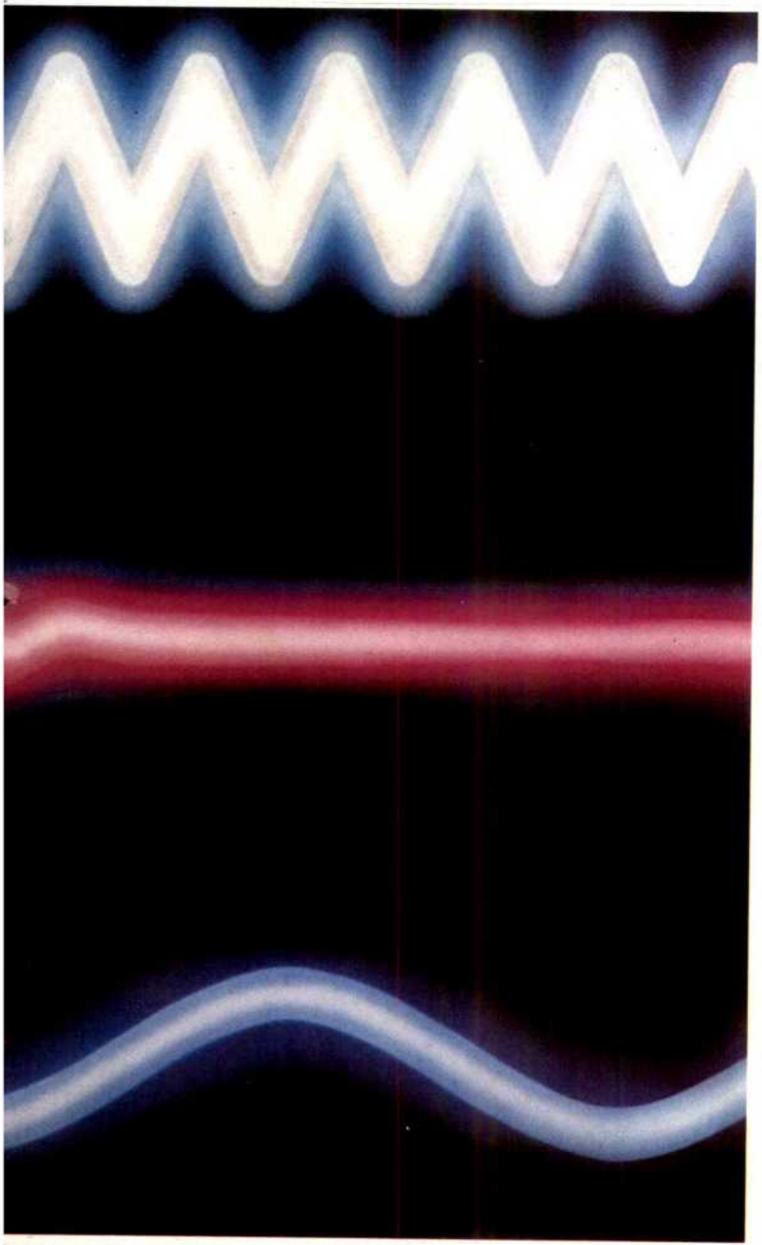

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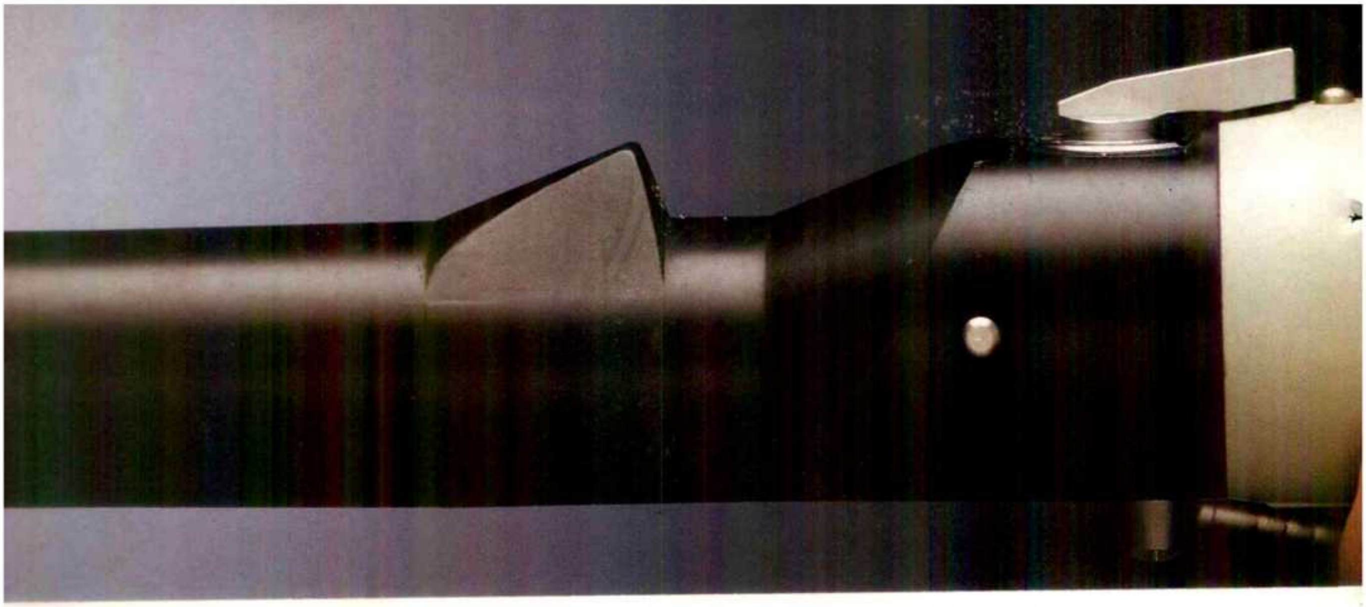

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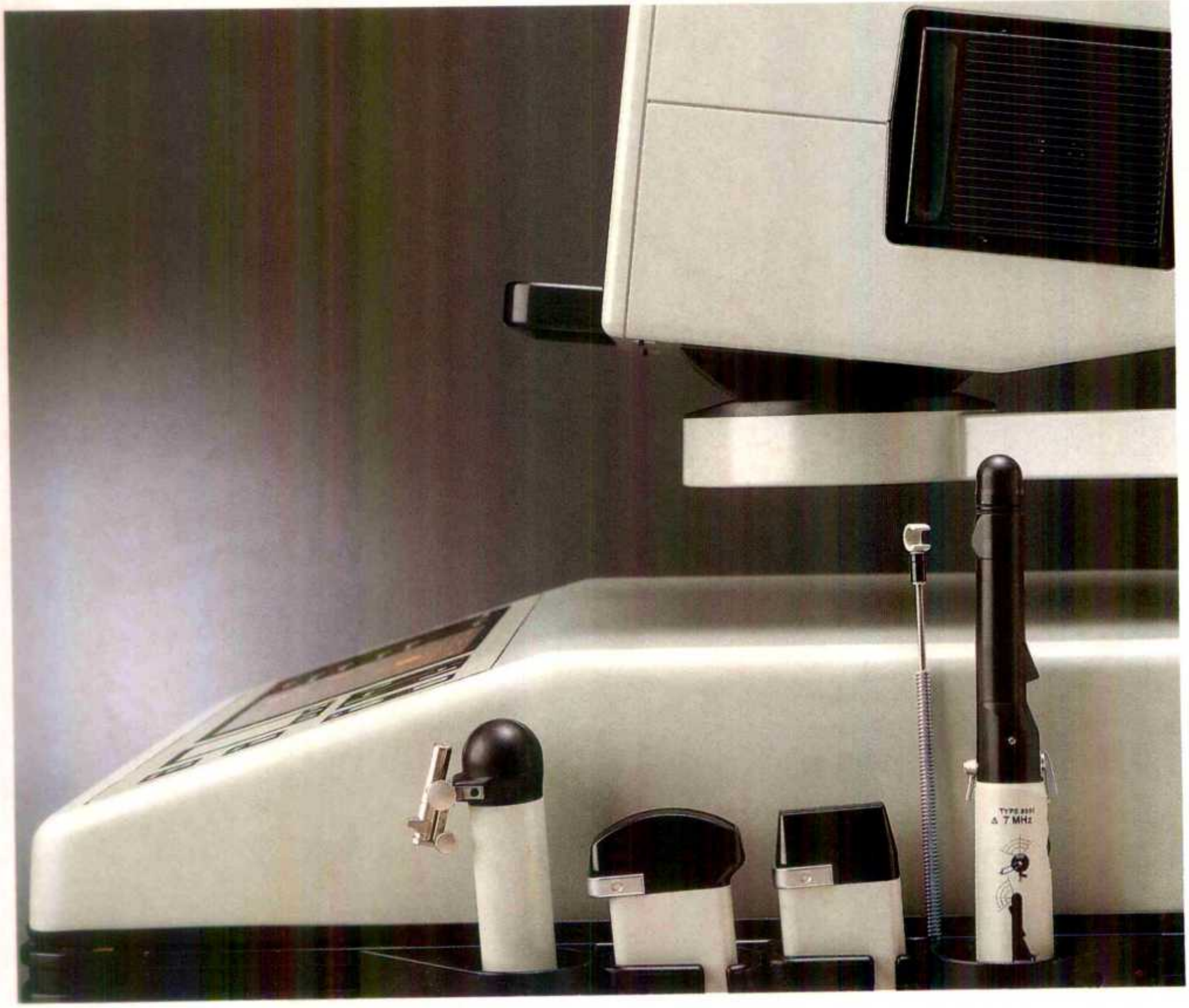

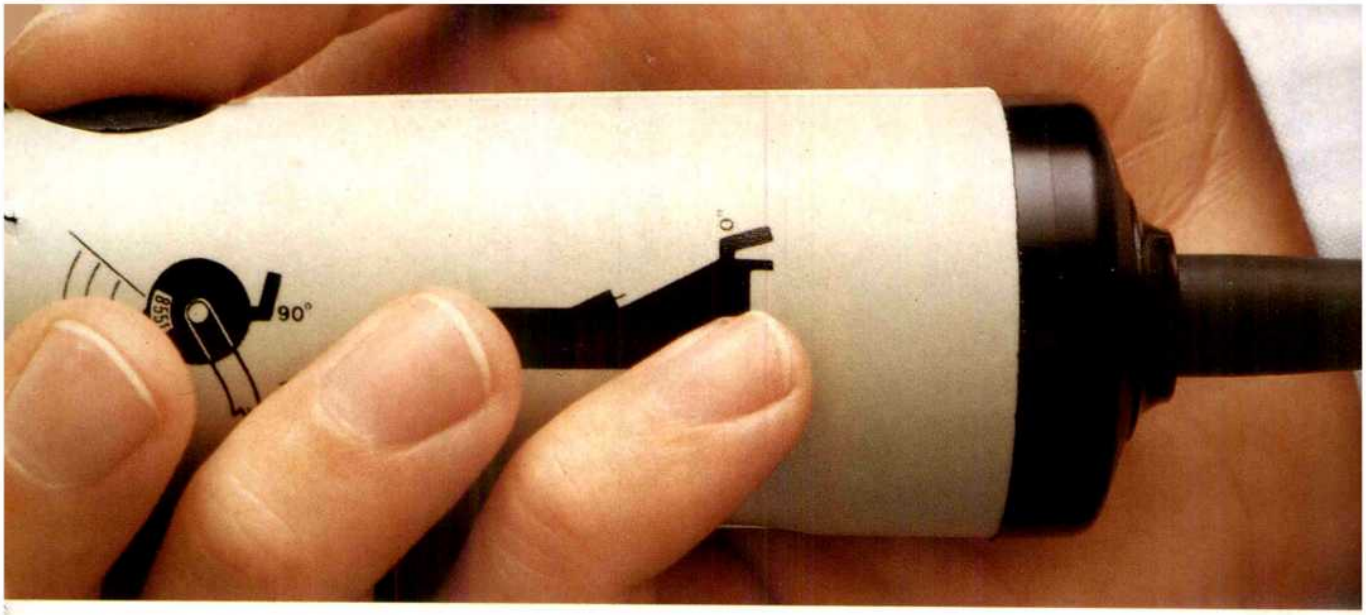

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Chest radiograph scoring system for use in pre-term infants

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Keywords: Chest radiograph, Lung function, Neonate, Pre-term

Abstract. A scoring system to characterize the pre-term infant's chest radiograph appearance has been evaluated. Chest radiographs taken at 1 month of age in 20 infants (median gestational age 27 weeks) were scored according to abnormalities of lung volume, presence of opacification, interstitial changes and cystic elements (maximum score 17). The median score was 4 (range 1–14); the highest scores were for the only infants with cystic elements and/or interstitial changes on their chest radiographs. The scoring system documented accurately the severity of neonatal respiratory distress; the highest scores occurred in those infants requiring the most prolonged respiratory support, *i.e.* ventilated beyond 1 week of age ($p < 0.01$) and oxygen-dependent beyond 1 month ($p < 0.01$). It was also a useful predictor of chronic respiratory problems, with an 88% sensitivity in the detection of infants with the most severe lung function abnormalities at 6 months of age.

The neonatal chest radiograph can be used to assess the severity of progression of respiratory distress syndrome (RDS) (Giedion et al, 1973; Kero & Makinen, 1979). Unfortunately, although this correlates with clinical severity it is not a reliable predictor of either survival (Kanto et al, 1978) or the development of bronchopulmonary dysplasia (Sinkin et al, 1990). The radiographic appearance, however, may be further classified by use of scoring systems (Toce et al, 1984). Amongst infants requiring mechanical ventilation, the use of such a scoring system improves the correlation with clinical status. We have developed a scoring system (presented to the British Paediatric Association in 1989) which classifies the chest radiograph appearance at 1 month of age and demonstrated this has good predictive ability, in that it had a high sensitivity and specificity to detect infants who remained chronically oxygen-dependent beyond 36 weeks post-conceptional age. Fortunately this severity of chronic lung disease is uncommon, but many premature infants have lung function abnormalities at follow-up (Yuksel et al, 1991) and, as a consequence, sufffer from recurrent respiratory symptoms (Greenough et al, 1990) and may even need re-admission to hospital (Sauve & Singhal, 1985). Identification of infants at risk of such respiratory morbidity, at a stage when intervention strategies may successfully prevent or reduce further lung damage, is thus highly desirable. The aim of this study was to determine whether our scoring system of the chest radiograph appearance at 1 month of age was a useful predictor of lung function abnormalities at follow-up.

Methods

Consecutive very low birthweight (VLBW) pre-term infants were entered prospectively into the study if they had had a chest radiograph taken at 1 month of age for clinical purposes. The appearance of these chest radiographs was related to the requirement for respiratory support in the neonatal period and the results of lung function measurements at 6 months of age.

The antero-posterior chest radiograph, taken in the supine position, was evaluated and the appearance scored by a paediatric radiologist (J.K.) unaware of clinical details of the individual patients. The chest radiograph scoring system had originally been devised by assessment of 50 chest radiographs by two paediatric radiologists (J.K. and A.P.) and then refined by evaluation of a further 40 chest radiographs. The chest radiograph is scored according to the size of the lung volume, the presence of opacification, interstitial changes or cystic elements (Table I). Lung inflation was defined by reference to the rib configuration and height of the diaphragm, overinflation being indicated by widely spread and horizontal ribs and underinflation by the ribs being close together with a vertical configuration. Opacification was indicated by loss of the silhouette of the mediastinum and/or diaphragm. An air bronchogram was only deemed present if demonstrated in the outer third of the lung field and was defined as delineation of air-filled bronchi by surrounding fluid-filled or collapsed alveoli. Interstitial shadows were defined as linear or nodular densities of focal areas within the lungs without a normal anatomical origin. The presence of interstitial shadows was scored on a zonal basis, the chest being divided into four zones (right and left, upper and lower) (Chrispin & Norman, 1974). Cysts were defined as lucent intraparenchymal lesions with a well circumscribed margin. The range of scores is from 0 to 17, a score of 17 indicating the most abnormal appearance (Figs 1 and 2).

The reproducibility of the scoring system was determined by the two radiologists independently scoring 50

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Table I. Chest radiograph scoring system

	Score				
	0	1	2	3	4
Volume of thorax	Normal	Decreased	Increased		
Degree of inflation of lung fields	Normal	Underinflated	Overinflated		
Opacification	Absent	Perihilar *or* regional	Perihilar *and* regional	Complete opacification	
Air bronchogram	Absent	Present			
Pulmonary interstitial emphysema	Absent	Present			
Interstitial changes (coarse shadowing)	Absent	Present in one zone	Two zones	Three zones	Four zones
Cystic element	None	Single	Multiple		
Size of largest cyst	None (not applicable)	Up to one-third of ipsilateral lung field	Larger than one-third of ipsilateral lung field		

chest radiographs. The chest radiographs were all taken at a post-natal age of 1 month in a group of pre-term infants who had a median gestational age of 29 weeks (range 24–37 weeks) and birthweight 1.23 kg (range 0.5–3.41 kg). The mean difference between paired scores was 0.05 with a standard error of 0.38.

All pre-term infants born at King's College Hospital (KCH) routinely have lung function measurements in the Paediatric Respiratory Laboratory at 6-monthly intervals during the first 2 years of life. Lung function is assessed by measurement of thoracic gas volume (TGV), airways resistance (Raw) and functional residual capacity (FRC). Infants are sedated with oral chloral hydrate (100 mg/kg) and lung function measured during quiet sleep in the supine position. TGV and Raw are measured using an infant whole-body plethysmograph. TGV is measured at the end of a normal inspiration and Raw at two-thirds of a maximum inspiratory flow by the classical techniques of Dubois et al (1956a,b) suitably modified for infants by Radford (1974). The coefficient of variation of TGV is 6% and for Raw 9%. After completion of the measurements of TGV and Raw, FRC is then assessed using a helium gas dilution technique. The coefficient of variation of this measurement is 7.3% (Yuksel et al, 1990).

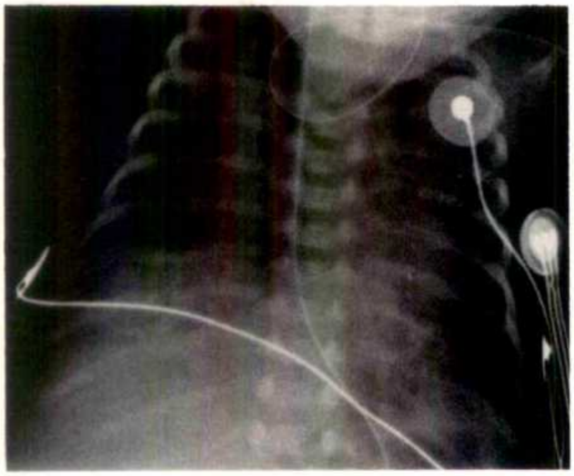

Figure 1. Chest radiograph score 6. The chest radiograph of a non-ventilated infant was performed at 29 days of age. The infant had been ventilated for 10 days and was in oxygen for a total of 60 days. The chest radiograph shows opacification with interstitial changes in the right and left lower zones. There are cystic changes in left lower and right upper zones. The cystic changes are less than one-third of the ipsilateral lung fields in diameter.

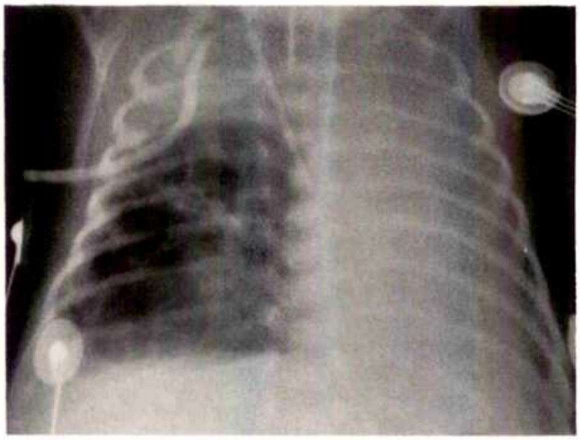

Figure 2. Chest radiograph score 12. The chest radiograph of this ventilated infant was performed at 30 days of age. The infant was ventilated for 40 days and was in oxygen for 51 days. The radiograph demonstrates underinflation with a reduced lung volume. There is collapse of the right upper lobe and left lung with overdistension of the right middle and lower lobes. There are opacifications (perihilar and regional) and interstitial changes in the right middle and lower zones. There are cysts in two zones of a size between one-third and two-thirds of the ipsilateral lung field. This infant subsequently underwent a right middle lobectomy.

Table II. Chest radiograph score related to lung function results. Results expressed as median values (ranges in parentheses)

	Chest radiograph score	
	< 4	$\geqslant 4$
Raw ($cmH_2O/l/s$)	23 (16–33)	36 (20–70)
FRC (ml/kg)	30 (25–39)	30 (23–42)
TGV (ml/kg)	40 (31–53)	37 (25–46)

Patients

Twenty pre-term VLBW infants (12 boys and eight girls) were entered into the study. The infants had a median birthweight of 1.046 kg (range 0.506–1.500 kg) and gestational age of 27 weeks (range 23–32 weeks). All the infants had suffered from respiratory distress syndrome (RDS), as evidenced by rapid distressed breathing with indrawing of the thoracic soft tissues, which did not recover within 24 h of birth and all causes other than surfactant deficiency being excluded. They had been ventilated in the neonatal period for a median duration of 7 days (range 1–42 days). The infants had been oxygen-dependent for a median of 18 days (range 2–128 days) and six were still oxygen-dependent at 1 month of age.

Ethical permission for this study was granted by the King's College Hospital Ethics Committee.

Statistical analysis

To assess if differences between the groups were statistically significant, the Wilcoxon Rank Sum test was used. The median chest radiograph score of the 20 infants was calculated and comparison made of the lung function results of infants with a radiograph score greater than or equal to the median and those with a score below it. The sensitivity and specificity of this score in predicting an abnormally high airways resistance [$> 32\ cmH_2O/l/s$, *i.e.* above the 95% confidence limits of the reference range (Radford, 1974)] were calculated.

Results

The median chest radiograph score was 4 (range 1–14). Five infants had chest radiograph scores above the median, ranging from 5 to 14. All 20 infants had opacification/haziness of the lungs and 15 had abnormalities of lung volume. Infants with the highest scores $\geqslant 6$ were the only infants who had cystic elements ($n = 4$) and/or interstitial changes ($n = 3$) present on their chest radiographs. The two infants with the highest scores (12 and 14) both subsequently underwent lobectomy for gross cystic degeneration following localized severe pulmonary interstitial emphysema.

The 10 infants ventilated for longer than 1 week had a worse radiograph score (median 5, range 3–14) than those ventilated for between 1 and 7 days (median 3, range 1–4), $p < 0.01$. Infants who remained oxygen-dependent at 1 month of age had a worse chest radiograph appearance score (median 7, range 4–14) than those oxygen-dependent at 1 month (median 4, range 1–5), $p < 0.01$.

There was no significant difference in either the median TGV or FRC between infants with a high or low chest radiograph score. Airways resistance, however, was significantly higher in those infants with a score $\geqslant 4$ ($p < 0.05$) (see Table II). A chest radiograph score of 4 had a sensitivity of 88% and a specificity of 54% in detecting an abnormally high airways resistance.

Discussion

Comparison of infants with a high and low chest radiograph score revealed that the former group had significantly elevated airways resistance. There was no difference, however, in TGV or FRC between the groups and indeed the majority of infants had lung volumes within the expected range (Stocks & Godfrey, 1976). These results are similar to our previous findings (Yuksel et al, 1991); although elevation of airways resistance is common at follow-up of pre-term infants, only those with severe bronchopulmonary dysplasia have persistent abnormalities of lung volume.

The distinct series of radiographic changes of bronchopulmonary dysplasia, originally described by Northway et al (1967), in infants chronically dependent on respiratory support, is now uncommon and hence has been recently denoted Type II chronic lung disease (CLD) (Hyde et al, 1989). Type II CLD is usually complicated by pulmonary interstitial emphysema and has a poor prognosis, being associated with both a high mortality and prolonged requirement for supplementary inspired oxygen. It has been suggested that now the most common radiograph appearance is of homogeneous or patchy ill defined opacification in the lungs without coarse reticulation, now denoted as Type I CLD and is associated with complete resolution. The findings of the present study confirm those of Hyde et al (1989), in that, although all infants at 1 month of age had abnormalities of their chest radiograph appearance, in the majority the changes were mild and would fall into the group they had classified as Type I CLD. We can also confirm that this radiograph appearance is associated with a good prognosis, as all the infants we studied were not oxygen-dependent at 6 months of age.

Opacification was found on the radiographs of all infants studied. It has been suggested that opacification represents oedema and thus will resolve (Mortensson et al, 1989). The results of the present study confirm this hypothesis, as infants with a low radiograph score on whose radiographs there was opacification without interstitial shadows or cystic elements had an airways resistance within the normal range (Radford, 1974; Stocks & Godfrey, 1976) at 6 months of age.

We included in this study only a proportion of preterm infants, as they were selected by a clinical need for a chest radiograph at 1 month of age. As apparently asymptomatic infants were excluded from our study, we cannot say if chest radiograph abnormalities at this age are compatible with no respiratory symptoms. By including infants symptomatic at 1 month and many who were still oxygen-dependent, we were, however, assessing a group of infants now classified as suffering from CLD (Bancalari et al, 1979) and thus most likely to have chronic respiratory problems. It is in this group, therefore, that prediction of chronic lung function abnormalities would be most useful.

The chest radiograph scoring system used in the present study has a high reproducibility, which compares favourably with previous systems (Edwards et al, 1985). Our results suggest it will be particularly useful because, as in previous systems (Palta et al, 1990), it accurately documents the severity of neonatal respiratory distress, the highest scores being found in infants who required the most prolonged respiratory support, but it is also a sensitive predictor of chronic lung function abnormalities.

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Computed tomography attenuation measurements for the characterization of hepatic haemangiomas

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Keywords: X-ray computed tomography, Haemangioma, Liver neoplasms

Abstract. The attenuation values of 21 hepatic haemangiomas in 19 patients were measured on non-enhanced computed tomographic (CT) scans and compared with the attenuation of adjacent liver and the inferior vena cava (IVC). The attenuation of hepatic haemangiomas was lower than that of the surrounding liver, but there was no correlation between these two measurements. There was a highly significant correlation between the attenuation of haemangiomas and blood in the vena cava ($r = 0.905$, $p < 0.001$). All the haemangiomas had attenuations within 7 HU of caval blood. By comparison, in 34 hypodense hepatic lesions that did not show contrast-enhanced appearances characteristic of haemangioma, there was no significant correlation between the attenuation of the lesions and the IVC. Nineteen (56%) of these lesions had attenuations differing more than 7 HU from that of caval blood. The influence of this observation on the requirement for dynamic contrast-medium-enhanced and delayed post-contrast CT in the assessment of hepatic lesions is discussed.

Several characteristic computed tomographic (CT) features of hepatic cavernous haemangiomas have been recognized for over a decade (Freeny et al, 1979; Barnett et al, 1980; Itai et al, 1980). Typically, they are hypodense compared with surrounding liver on the unenhanced CT scan. Significant peripheral enhancement occurs during dynamic contrast-medium-enhanced scanning. Later they "fill in" centripetally with contrast medium to become isodense with liver on delayed post-contrast scanning, though this may take up to an hour. Clefts of non-enhancement within the lesion may be present, particularly in the larger lesions described as giant cavernous haemangiomas (Scatarige et al, 1987; Choi et al, 1989). The time required for isodense "fill-in" to occur should not be less than 3 min from the injection of contrast medium. Whilst this description has a 100% positive predictive value for haemangiomas (Ashida et al, 1987), Freeny and Marks (1986a) found only 55% of haemangiomas fulfilled these criteria and also calculated that in patients with known malignant disease, only 86% of lesions with this appearance would be haemangiomas (Freeny & Marks, 1986b).

Two previous publications describe hepatic haemangiomas as having similar pre-contrast attenuation to that of blood (Itai et al, 1980, 1983), but these studies did not substantiate this with attenuation measurements. The present study was undertaken to evaluate this observation quantitatively and to assess its application in practice.

Patients and methods

In a retrospective study of the 4-year period from March 1986 to May 1990, 19 patients with 21 hepatic haemangiomas had been examined by CT in the Department of Diagnostic Radiology. The diagnosis was based on the CT demonstration of a lesion of lower attenuation than surrounding liver, which showed peripheral enhancement on dynamic contrast-medium-enhanced CT and became isodense with surrounding liver on delayed post-contrast scanning. These features were present in all patients. Fifteen patients also had ultrasound examinations, which revealed well defined hyperechoic lesions. Biopsy confirmation was available in five patients. Clinical follow-up of between 6 months and 4 years confirmed the benign nature of all the hepatic haemangiomas. There were six men and 13 women, with ages between 31 and 77 years (mean 52 years).

In a further 13 patients who were scanned for assessment of histologically proven malignant disease, 34 other hepatic lesions were identified. These patients had pre- and post-contrast studies and were diagnosed as having multiple hepatic metastases on the basis of clinical findings, follow-up, liver ultrasound scan and abdominal CT.

All patients were scanned on a GE 9800 general-purpose CT scanner. The pre-contrast-medium scans from these patients were interrogated on an independent console; a section through the middle of each hepatic lesion was chosen and an oval region of interest (ROI) was placed to include the largest possible area within each lesion, allowing at least a 5 mm margin to prevent partial volume averaging from surrounding liver (Fig. 1). The area and attenuation of this ROI was recorded. A similar region within the inferior vena cava (IVC) was chosen, with a smaller margin (approximately 1–2 mm) as the orientation of the IVC makes partial volume averaging with surrounding tissue unlikely. The attenuation of a representative region of adjacent hepatic parenchyma was also measured.

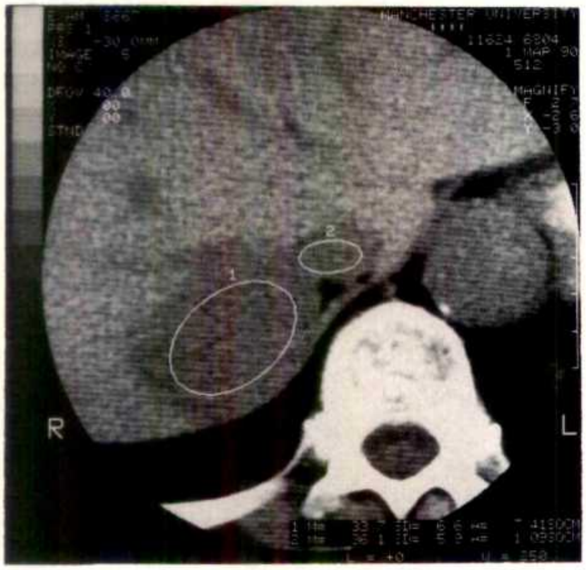

Figure 1. Typical pre-contrast CT scan of hepatic haemangioma demonstrating ROI choice for haemangioma (1) and IVC (2).

Results

The area of the haemangiomas varied from 0.61 cm^2 to 15 cm^2 (mean 3.74 cm^2). There was no significant difference in the results of attenuation values or correlation with blood attenuation for small lesions (less than 1 cm^2) compared with large lesions. The results have therefore been combined. Haemangiomas had a significantly lower mean pre-contrast attenuation (38.3 ± 7.1 HU) than surrounding liver (57.5 ± 5 HU) ($p < 0.0001$), but showed no correlation with liver attenuation.

Haemangiomas had similar mean attenuation to blood in the IVC (37.7 ± 6.2 HU) and a significant correlation was evident between these measurements ($r = 0.905$, $p < 0.001$) so that all haemangiomas lay within 7 HU of blood attenuation (Fig. 2).

All the hepatic lesions in patients with malignant disease were hypodense when compared with surrounding liver (mean = 30 ± 8.8 HU), but showed no significant correlation with liver or IVC attenuation ($r = 0.26$). Fifteen of the 34 lesions (44%) had attenuations within 7 HU of blood. The distribution of attenuation values relative to the IVC in these patients is demonstrated in Fig. 3. None of these lesions showed

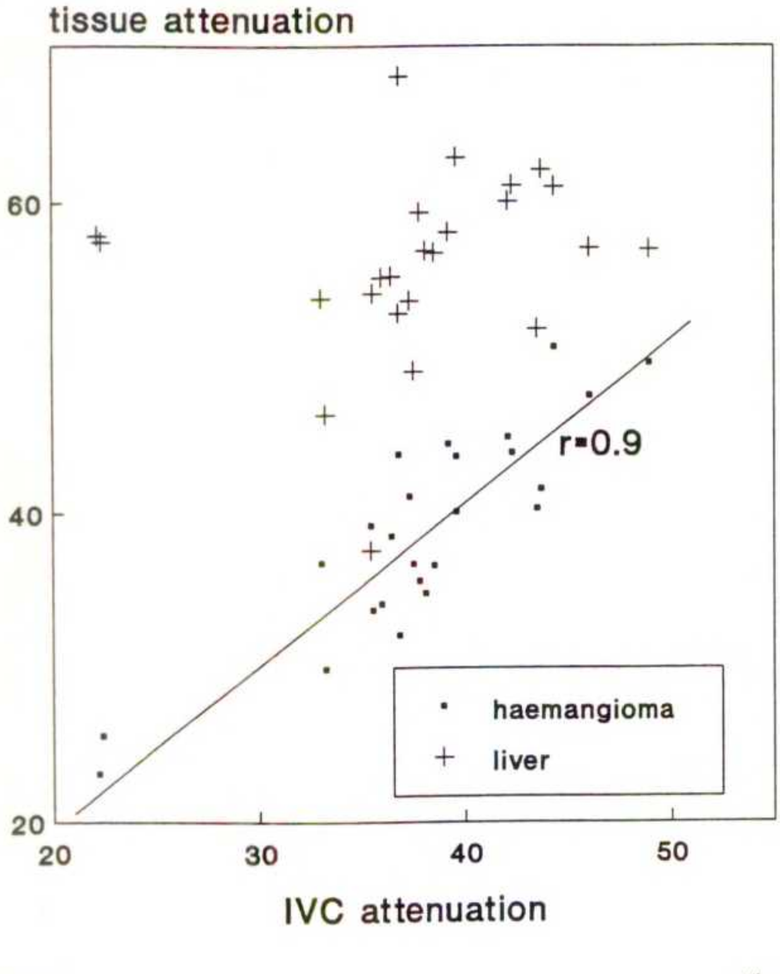

Figure 2. Pre-contrast CT attenuation values for liver and hepatic haemangiomas plotted against attenuation values for the inferior vena cava content on the same section.

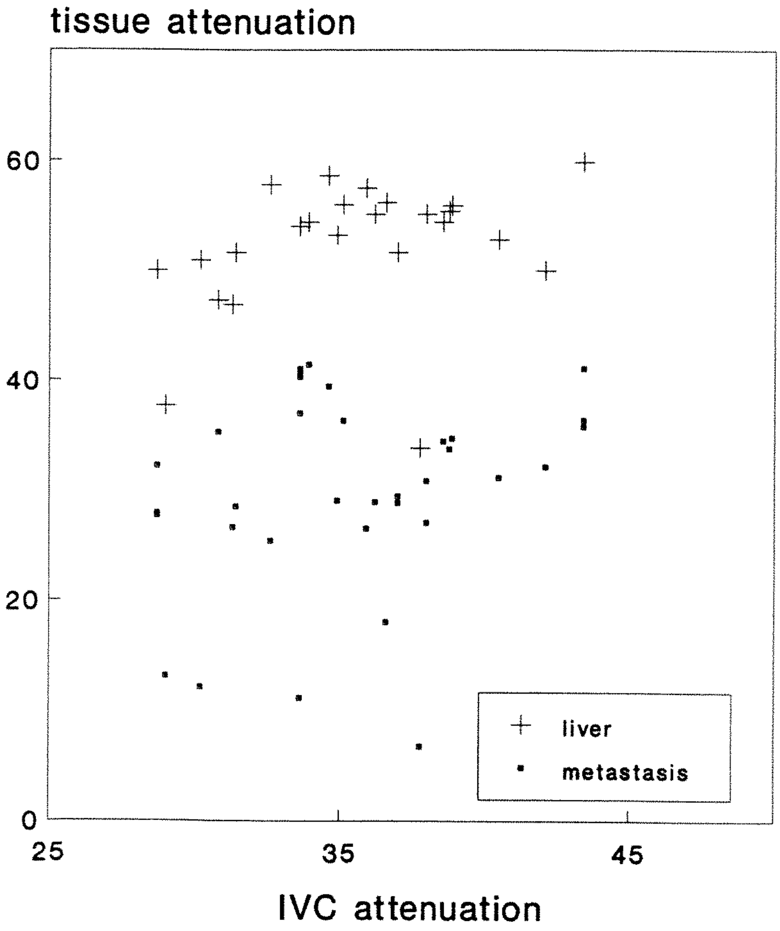

Figure 3. Pre-contrast CT attenuation values for liver and hypodense hepatic lesions plotted against attenuation values for the inferior vena cava contents on the same section.

the dynamic contrast-medium-enhanced CT appearances typical of haemangiomas.

Discussion

Histologically, hepatic cavernous haemangiomas are composed of large vascular spaces with thin areas of stroma and occasional hepatocytes. Cystic change, haematoma and fibrosis may occur in larger haemangiomas, with consequent change in CT appearances (Takayasu et al, 1986). Most smaller haemangiomas, however, have consistent CT appearances as described in the introduction. It should not therefore be surprising that the CT attenuation of a haemangioma is similar to that of blood, as this is the largest component by volume.

Despite the potential difficulties in obtaining accurate attenuation measurements from CT scans owing to beam hardening, motion artefacts and other factors, this study demonstrates that practically useful results can be obtained by using a relevant intrinsic tissue as a reference. Where CT attenuation numbers are obviously inaccurate due, for example, to streak artefacts or beam hardening, then no measurement of attenuation, either absolute or relative to other parts of the same scan, will be of great value. In the present study this did not pose a problem in the assessment of hepatic lesions, probably because of the large size and uniform nature of the liver. Peripheral lesions or scans of reduced quality should, however, be interpreted with care.

Whilst the use of the unenhanced, post-contrast and dynamic contrast-medium-enhanced appearances of hepatic lesions as criteria for diagnosis of a haemangioma in this study places limitations on the interpretation of the results, as none of these patients have developed evidence of malignant disease, then these appearances are approximately 100% specific for haemangioma (Ashida et al, 1987; Freeny & Marks, 1986a,b). Haemangiomas with attenuation values similar to, or higher than, surrounding liver are unusual but may occur in livers that have fatty infiltration or in patients with high haematocrits. Although no such lesions were included in the present study, three haemangiomas were within 10 HU of liver attenuation. Previous publications have described haemangiomas in fatty infiltrated livers (Ashida et al, 1987; Freeny & Marks, 1986a,b) noting them to be of higher attenuation than surrounding liver. No satisfactory modification to the CT description of hepatic haemangioma was suggested by these authors to allow for this. By extrapolation from the current findings, an altered definition of the pre-contrast appearances of haemangiomas would allow lesions to be included if they lay within 7 HU of the IVC attenuation, whatever the relationship to hepatic attenuation.

Several different techniques for CT liver scanning have been described, the choice of technique being largely determined by the clinical circumstances (Ferrucci et al, 1988). Typical appearances on unenhanced scans, dynamic contrast-enhancement and delayed post-contrast-medium scans are required for a CT diagnosis of hepatic haemangioma. The usual clinical circumstance in which this series of scans is performed is in the further evaluation of a patient with a solitary hepatic mass, where the differential diagnosis includes metastatic tumour and haemangioma. Currently, any incidental hepatic lesion of lower attenuation than surrounding liver on unenhanced CT is thus potentially a haemangioma, and requires dynamic intravenous contrast enhancement for further CT evaluation, followed by delayed post-contrast scanning if peripheral enhancement is evident on the dynamic scans. The results of this study suggest that such further evaluation will only be positive (typical of a haemangioma) if the attenuation of the unenhanced lesion lies within 7 HU of the IVC. As blood and most hepatic metastases are of lower attenuation than surrounding liver, a range of 7 HU each side of blood attenuation may still incorporate a large proportion of lesions that will not show characteristic contrast enhancement (44% of those measured in this study, none of which were subsequently identified as haemangiomas). However, by the same argument, such enhancement may be confidently excluded in the 56% of cases with lesions more than 7 HU away from caval blood on the unenhanced scans, obviating the need for contrast studies in these patients.

The results of these quantitative measurements made in hepatic lesions suggest that comparison of attenuation in hepatic lesions and the IVC may provide criteria by which the need for performing additional contrast-medium-enhanced scans be judged.

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Comparative performance *in vitro* and *in vivo* of Lunar DPX and Hologic QDR-1000 dual energy X-ray absorptiometers

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Abstract. The measured absolute bone mineral density values of spine and femur and their precision were compared on two dual energy X-ray absorptiometers, the Lunar DPX and the Hologic QDR-1000. There were systematic differences between the two systems, the Lunar DPX always giving a higher bone density value. The ratio of the mean Lunar DPX/Hologic QDR-1000 bone density measurements obtained *in vivo* was 1.13 g/cm^2 for spine (L2–L4) and 1.20–1.43 g/cm^2 for femur measurements. For both systems, short- and long-term precision (coefficient of variation) was below 0.5% for spine *in vitro* measurements and below 1.5% for neck of femur *in vitro* measurements. Precision of *in vivo* measurements was less good, especially for femur measurements. The coefficient of variation of spine measurements was dependent on bone density and deteriorated with decreased bone mineral density and increased body thickness.

Dual energy X-ray absorptiometry is used increasingly for the detection and management of osteoporosis (Mazess & Barden, 1989). This technique is quick and non-invasive. It has a low radiation dose and can measure bone density in clinically important sites such as the spine and femur. Several dual energy X-ray absorptiometers are commercially available. They use different software and different methods of producing the two X-ray spectra. We have compared the performance of the Lunar DPX with the Hologic QDR-1000 system using identical phantoms and patient groups.

Methods

The Lunar DPX and the Hologic QDR-1000 dual energy X-ray absorptiometers

The Lunar DPX and Hologic QDR-1000 scan subjects rectilinearly using X rays at two energies. The total bone mineral content of the trabecular and cortical bone in the lumbar spine or specific regions of the femur can be calculated in the presence of soft tissue from the attenuation of the X-ray beams by the subject (Cullum et al, 1989; Mazess et al, 1989). Figure 1 demonstrates the three regions of the femur investigated.

The two systems use different mechanisms to produce the X-ray spectra. The Lunar DPX uses a constant potential X-ray tube with a cerium K-edge filter to produce an X-ray spectrum with two components having mean energies of 38 and 70 keV. The dual energy measurements are made simultaneously with an energy-discriminating detector (Mazess et al, 1989). The Hologic QDR-1000 rapidly switches the tube potential to produce spectra with maximum photon energies at 45 keV and 100 keV, alternately. Measurements are made sequentially (Cullum et al, 1989). Areal bone

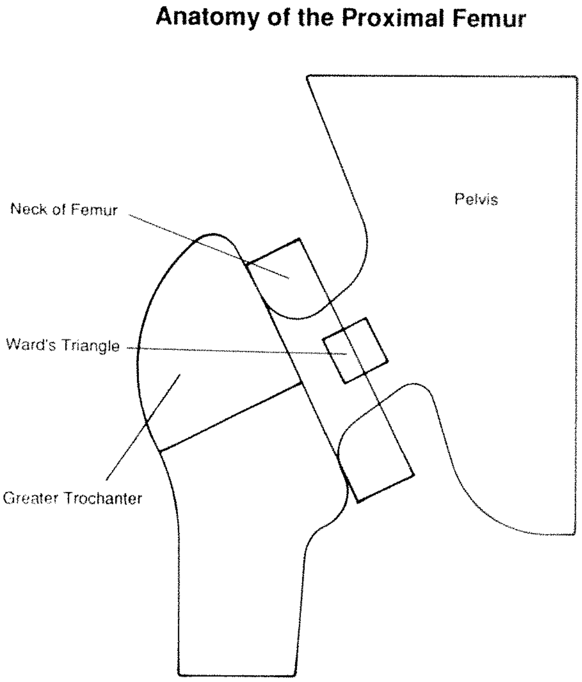

Figure 1. Diagram of the femoral head and neck to show the three regions of bone density measurement: (i) femoral neck, (ii) greater trochanter and (iii) Ward's triangle.

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mineral density (BMD) in g/cm^2 is calculated by dividing the bone mineral content (BMC) in grams by the area in cm^2 occupied by bone. On each machine software algorithms are available to determine the bone edge and the bone regions. Both systems have a facility to compare a subsequent image with the regions obtained from a previous analysis. The Lunar DPX has four scan speeds: detail (scan time 20 min); slow (10 min); medium (5 min); and fast (2 min). Only one scan time is available on the Hologic QDR-1000 (10 min). The pixel size on the images generated is 1.0 mm on the Hologic QDR-1000 and 1.2 mm on the Lunar DPX at the medium and slow scan speeds. The Lunar DPX fast and detail mode scans were not investigated in this study.

Radiation dose

The mean entry radiation dose of each bone densitometer was measured using lithium fluoride extruded ribbon thermoluminescent dosemeters. These were placed on the surface of an Alderson Rando tissue-equivalent phantom. The phantom was scanned 20 times on each machine; the medium speed was used for the Lunar DPX. As only a small proportion of the body is irradiated during a scan, the effective dose equivalent was calculated by estimating the radiation dose to a number of organs weighted according to a risk estimate for each organ concerned (ICRP, 1977). Allowance was made for the different penetration of the X rays used on the two machines using appropriate depth dose data (Jennings & Harrison, 1983).

In vitro studies

Comparison of absolute values. To compare the measurement of spine BMC with BMD, the Hologic spine phantom was scanned 46 times on both machines. The Hologic spine phantom consists of moulded vertebrae (simulating human L1–L4) embedded in a 17 cm high epoxy block. This phantom was also scanned upside down to determine whether subjects, unable to lie on their backs, could be scanned lying on their stomachs. To compare the measurement of regional femur BMC with BMD, the Lunar femur phantom was scanned 10 times in 15 cm of water on both the Lunar and Hologic machines. The Lunar femur phantom is a slab of aluminium in the shape of the femoral head (Fig. 1).

Long-term and short-term precision. To determine precision, in both the short- and the long-term, the Hologic spine phantom was scanned approximately daily on each machine over a period of 6 months. *In vitro* femur precision was determined by scanning the Lunar femur phantom 10 times in 15 cm of water on each machine on the same day without repositioning. Phantom scans were analysed using the compare facility.

Effect of changes in thickness on bone density. To determine the effect of subject thickness, the Lunar spine phantom was scanned 5–10 times on each machine in depths of water from 5 cm to 32 cm. The Lunar spine phantom is a rectangular slab of aluminium, with regions of varying density to represent L1–L4. The medium scan speed was used on the Lunar DPX for depths of water 5 cm to 22 cm and the slow scan speed for depths 24 cm to 32 cm. The Lunar DPX was unable to delineate correctly the edge of the spine phantom during the analysis for water depths greater than 22 cm. Therefore, the edges of these spine phantom images had to be adjusted manually before the bone density could be determined.

Linearity. Stacks of rectangular sheets of aluminium were used to determine the relationship between the amount of bone-equivalent material and the BMD determined on each machine. One to five identical sheets of aluminium, each 2 mm thick and of area 160.8 cm^2, were scanned in 15 cm of water, five times on each machine. The thicknesses were chosen to give measured BMD values which spanned the expected clinical range (0.5–1.5 g/cm^2).

In vivo studies

Comparison of absolute values of BMD. 50 non-obese subjects, volunteers and patients, referred for investigation for osteoporosis were studied. Their ages ranged from 26 to 72 years. Each subject's spine (L2–L4) and femur BMD were measured on both machines on the same day.

Precision. In order to measure precision *in vivo*, sets of duplicate spine and femur scans were performed on another group of non-obese subjects (aged 15–70 years). Altogether 24 pairs of measurements were obtained for each of the following combinations: Lunar spine; Lunar femur; Hologic spine; Hologic femur. Each pair of scans was performed on the same day. Between the scans the subject got off the bed and was repositioned for the second scan.

Statistical analysis

When many measurements were made on the same phantom, the sample standard deviation (SD) was defined as

$$\mathrm{SD} = \sqrt{\frac{\Sigma x^2 - (\Sigma x)^2 n^{-1}}{n-1}}$$

where n = number of observations and x = parameter measured. For *in vivo* precision when many duplicate measurements were obtained

$$\mathrm{SD} = \sqrt{\frac{\Sigma d^2}{N}}$$

where d = difference between duplicates and N = total number of separate determinations. Precision is given as coefficient of variation (CV)

$$\mathrm{CV} = \frac{\mathrm{SD} \times 100\%}{\bar{x}}$$

where $\bar{x}$ = mean.

The relationship between Lunar DPX and Hologic QDR-1000 values was examined by linear regression analysis and by the method of Bland and Altman (1986). For the latter method the difference between the two techniques was plotted against the mean of their values.

Results

Radiation dose

The energy-corrected surface dose was 11 μSv (SD = 2 μSv) for a 5 min (medium speed) scan on the Lunar DPX and 52 μSv (SD = 10 μSv) for a 10 min scan on the Hologic QDR-1000. The effective dose equivalent will be lower than the surface dose since only a small part of the body is irradiated. The effective dose equivalent was calculated to be 0.2 or 1.1 μSv for the Lunar DPX spine scan and 1.1 or 7.6 μSv for the Hologic QDR-1000 spine scan. The higher doses will apply for young women when the ovaries are taken into account. The figures for the Hologic QDR-1000 are broadly similar to those given by Pye et al (1990). Even allowing for differences in scan time, the Lunar DPX doses were significantly lower than Hologic QDR-1000 doses.

The scattered radiation from the Hologic QDR-1000 was measured as 1 μSv/h at 50 cm and as 0.3 μSv/h at 1 m in the direction of the consoles. For the Lunar DPX scatter was about 0.8 μSv/h at 50 cm.

In vitro studies

Comparison of absolute BMD values. Tables I and II show the mean and the SD for BMC, area and BMD of the Hologic spine phantom and the Lunar femur phantom, as measured by both systems. The Lunar system consistently gave higher BMD values both in the spine and femur. When the Hologic spine phantom was scanned upside down on either the Lunar DPX or Hologic QDR-1000, the mean BMC and BMD values were not significantly different from those values obtained by that system when the phantom was scanned the right way up. Thus, it may be possible to determine the bone densities of subjects unable to lie on their backs.

Precision. The short-term precision of all the spine phantom BMD measurements was less than 0.5%. For the Lunar DPX and Hologic QDR-1000, respectively, the short-term precision was 1.0% and 1.4% for the neck of femur phantom, 0.6% and 0.5% for the greater trochanter and 2.1% and 1.5% for Ward's triangle. Long-term precision for spine phantom measurements was 0.39% for the Hologic QDR-1000 and 0.41% for the Lunar DPX. Although the precisions were broadly similar on the two machines, the precisions of the Lunar DPX were obtained with a shorter scan time.

Table I. Comparison of values obtained by the Lunar and Hologic systems, using the Hologic anthropomorphic spine phantom (L1–L4)

	Lunar ($n = 46$)	Hologic ($n = 46$)	Lunar/Hologic ratio
Area (cm^2)	54.6 (0)	56.0 (0.17)	0.97
BMC (g)	62.8 (0.28)	57.1 (0.22)	1.10
BMD (g/cm^2)	1.15 (0.005)	1.02 (0.004)	1.13

Results are expressed as mean (SD).

Table II. Comparisons of values obtained by the Lunar and Hologic systems, using the Lunar femur phantom

	Lunar ($n = 10$)	Hologic ($n = 10$)	Lunar/Hologic ratio
Area (cm^2)			
Neck	4.29 (0.027)	4.64 (0.088)	0.92
Greater trochanter	18.7 (0.29)	15.8 (0.266)	1.19
Ward's triangle	2.04 (0.027)	1.10 (0.020)	1.86
BMC (g)			
Neck	4.17 (0.038)	3.95 (0.115)	1.06
Greater trochanter	22.2 (0.34)	16.3 (0.326)	1.36
Ward's triangle	1.75 (0.037)	0.66 (0.015)	2.65
BMD (g/cm^2)			
Neck	0.972 (0.010)	0.853 (0.012)	1.14
Greater trochanter	1.19 (0.007)	1.04 (0.005)	1.15
Ward's triangle	0.857 (0.018)	0.601 (0.009)	1.43

Results are expressed as mean (SD).

Effect of changes in soft tissue thickness. For both machines there was a gradual decrease in precision with increasing depths of water (Table III). Thus, for depths below 22 cm, the precision (coefficient of variation) of

Table III. Effect of different depths of water on BMD of Lunar spine phantom

Water depth (cm)	Lunar		Hologic	
	BMD as % BMD @ 15 cm	%CV	BMD as % BMD @ 15 cm	%CV
5	unmeasurable		98.5	0.10
10	unmeasurable		98.5	0.33
13	99.9	0.32	99.9	0.10
15	100.0	0.34	100.0	0.75
17.5	100.4	0.42	100.5	0.42
20	100.6	0.61	100.8	0.41
22	100.6	0.44	100.9	0.64
24	100.2	0.76	not determined	
26	101.4	1.09	101.1	1.07
28	101.2	1.60	not determined	
30	98.2	2.77	98.8	2.05
32	unmeasurable		102.1	2.21

Table IV. Comparison of values obtained *in vivo* by the Lunar and Hologic systems, expressed as the Lunar/Hologic ratio ($n = 50$)

	Area (cm^2)	BMC (g)	BMD (g/cm^2)
Spine (L2–L4)	0.92	1.05	1.14
Neck of femur	0.91	1.10	1.20
Greater trochanter	1.10	1.35	1.20
Ward's triangle	2.50	3.58	1.43

both machines *in vitro* was less than 0.76%. This precision deteriorated to more than 2% for depths above 30 cm. Using Vernier callipers the area of the Lunar spine phantom was measured as 50.8 cm^2, midway between the values calculated by the Lunar DPX (50.2 cm^2, SD = 0.19 cm^2) and Hologic QDR-1000 (51.2 cm^2, SD = 0.17 cm^2). The measured area, BMC and BMD values obtained at each depth were normalized to the mean value at the 15 cm depth. The Hologic QDR-1000 measured the BMD to within 2% of the reference value at depths of water from 5 cm to 30 cm and the Lunar DPX at depths from 13 cm to 30 cm (Table III). For the Lunar DPX it was impossible to analyse scans performed at water depths below 13 cm and above 30 cm. Also on the Lunar DPX, manual adjustment of bone edges was required at depths of water above 22 cm. For both systems there was a slight increase in BMD with increasing depth of water up to 28 cm.

Linearity. Both machines were linear for the BMD range of 0.36 g/cm^2 to 1.8 g/cm^2 (clinically expected range 0.5–1.5 g/cm^2). Linearity was best for BMC and both machines were slightly less accurate for area at very low BMDs. The area of the aluminium slab was slightly underestimated (97% of area measured by Vernier callipers) at low BMDs and overestimated (101%) at high BMDs, both by the Lunar DPX and Hologic QDR-1000. During the analysis of scans, manual adjustment of bone edges was essential on the Lunar DPX for bone densities below 1.0 g/cm^2.

In vivo studies

Comparison of absolute BMD measurements. When assessed by linear regression analysis, high correlations were obtained between BMD values produced by the two machines at all sites of measurement (r = 0.92–0.99). However, as with the *in vitro* measurements, the Lunar DPX consistently gave higher values when compared with the Hologic QDR-1000 (Table IV).

It was felt more appropriate to investigate the agreement between the two systems using the method of Bland and Altman (1986). When the difference between

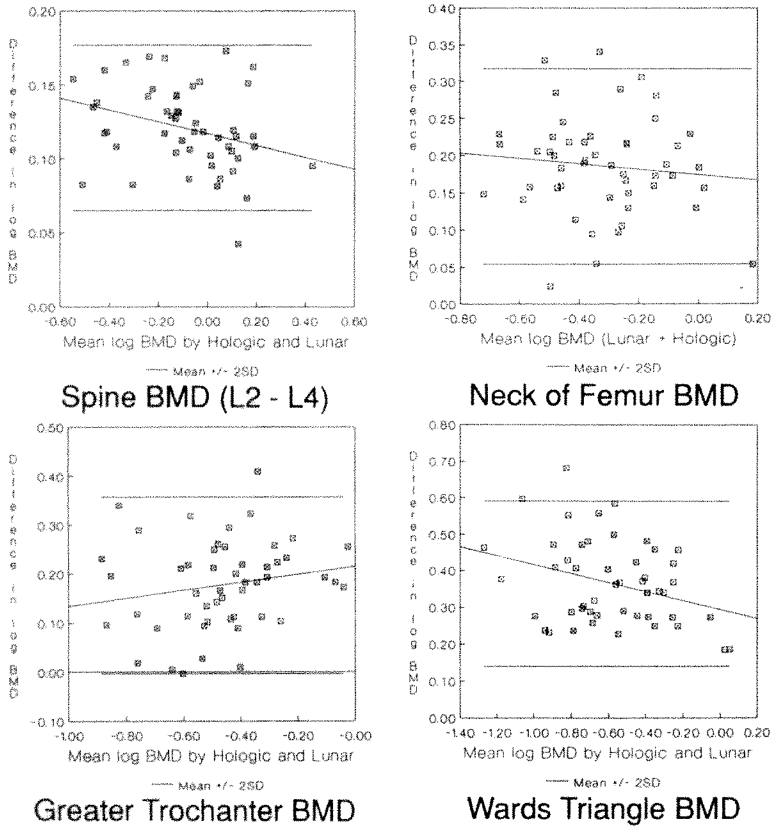

Figure 2. *In vivo* Lunar–Hologic BMD against mean BMD data after natural logarithmic transformation.

Table V. *In vivo* precision of spine and femur BMD measurements

	Lunar ($n = 24$)			Hologic ($n = 24$)		
	Mean BMD (g/cm^2)	SD (g/cm^2)	CV (%)	Mean BMD (g/cm^2)	SD (g/cm^2)	CV (%)
Spine (L2–L4)	1.01	0.012	1.2	0.91	0.009	1.0
Neck of femur	0.87	0.022	2.5	0.69	0.011	1.6
Greater trochanter	0.73	0.016	2.2	0.60	0.009	1.5
Ward's triangle	0.76	0.028	3.7	0.50	0.015	3.0

the two systems was plotted against their means, the Lunar–Hologic difference was found to increase as BMD increased. As the measurements varied in a systematic way over the range of measurements, a logarithmic transformation of the data had to be applied (Bland & Altman, 1986). Figure 2 shows the log-transformed data. For measurements in the spine and in Ward's triangle there was still a low but significant correlation between the difference and the mean BMD ($r = 0.305$, $p < 0.05$ and $r = 0.317$, $p < 0.05$, respectively). For the femoral neck and greater trochanter measurements no significant correlation was found ($r = 0.108$ and $r = -0.185$, respectively). The Lunar/Hologic bias (95% confidence limits) was 1.13 (1.07–1.19) for the spine. In the femoral neck, trochanter and Ward's triangle the corresponding bias values were 1.20 (1.06–1.37), 1.20 (1.00–1.43) and 1.44 (1.15–1.81), respectively. The bias calculated this way is similar to the crude Lunar/Hologic ratio given in Table IV. However, in quoting a single figure the more complicated relationship between the two measurements is masked.

Precision. Table V shows the BMD precision for *in vivo* measurements using the two machines. The precision was best for spine measurements and worst for measurements of Ward's triangle. The spine precisions were similar on the two systems. The femur precisions were somewhat worse on the Lunar DPX.

In order to assess the variation of precision with the value of BMD, the sets of paired measurements were divided into two groups. One group included subjects with BMD values in the lower half of the range and a second group included subjects with BMD values in the upper half of the range. The data divided in this way are shown in Table VI. The SDs were generally similar for the 'low BMD' and 'high BMD' groups measured on the Hologic QDR-1000. The SDs for the Lunar DPX were more variable and a consistent pattern could not be identified. When precision was expressed as coefficient of variation, it was worse for the 'low BMD' groups than the 'high BMD' groups on both machines, except for some Lunar DPX femur measurements.

Both machines have a compare analysis facility. This facility allows one to display a subject's previous scan image alongside the current image. This is supposed to increase the precision of measurements by decreasing the variability of operator analysis. There was no consistent improvement in precision on either machine when the data were analysed using the compare facility. All the data quoted in Tables V and VI were obtained by analysing the pairs of scans independently.

When scans were analysed separately by two trained

Table VI. Effect of BMD on spine and femur *in vivo* precision

	Lunar			Hologic		
	Mean BMD (g/cm^2)	SD	%CV	Mean BMD (g/cm^2)	SD	%CV
Spine (L2–L4)						
Low BMD	0.84	0.015	1.8	0.77	0.008	1.1
High BMD	1.15	0.007	0.6	1.09	0.009	0.8
Neck of femur						
Low BMD	0.74	0.015	2.0	0.59	0.010	1.7
High BMD	1.01	0.025	2.5	0.82	0.012	1.4
Greater trochanter						
Low BMD	0.61	0.016	2.6	0.50	0.009	1.9
High BMD	0.87	0.015	1.7	0.69	0.009	1.3
Ward's triangle						
Low BMD	0.60	0.023	3.1	0.38	0.014	3.7
High BMD	0.92	0.035	4.7	0.63	0.016	2.6

operators, virtually identical results were obtained for the spine scans on both machines and for the femur scans on the Hologic QDR-1000. Interobserver and intraobserver variation was less good for analysis of Lunar femur scans (CV up to 5%).

Discussion

Our results confirm previous reports demonstrating the low radiation dose, good linearity and high *in vitro* precision of BMD measurements by dual energy X-ray absorptiometry (Mazess et al, 1989; Sartoris & Resnick, 1989). We have taken the opportunity to compare the performance of two different systems both *in vitro* and *in vivo* and found systematic differences between them.

Our findings are consistent with the results of Gundry et al (1990), showing that the Lunar DPX gave consistently higher BMD values than the Hologic QDR-1000. In this previous study (Gundry et al, 1990), the relationship between measurements obtained on the two systems was examined by linear regression analysis. However, this method has a number of limitations. For example, although the correlation coefficient assesses the strength of the relationship between two techniques, it is a poor indicator of the agreement between them. We have used the method of Bland and Altman (1986) on the paired *in vivo* data to compare the two techniques. It is clear from Fig. 2 that there is a bias between the two techniques. In addition, in the case of the spine and Ward's triangle measurements, even after the log-transformation of the data, there was still a systematic trend in the difference between the measurements over the range of BMD investigated.

The reasons for the systematic differences observed in the absolute values between the two systems have not been fully clarified. A major factor is likely to be differences in calibration, the Hologic QDR-1000 being based on hydroxyapatite alone whilst the Lunar DPX incorporates a correction factor for intraosseous fat (Laval-Jeantet et al, 1986; Crawley et al, 1988; Gundry et al, 1990). Other factors which may contribute to the discrepancy in BMD values include differences in edge detection, areas measured and the different approach to dual energy production in the two systems. The implications of our results are that absolute BMD values from one system cannot be used interchangeably with those from another without careful allowance for the systematic differences. Absolute BMD values in isolation should not be used to determine prophylactic or therapeutic strategies for osteoporosis (Johnston et al, 1989). However, if the BMD values are related to appropriate reference range data, for example by using Z-scores (Parfitt, 1990), it should be possible to use either machine to define osteopenia.

In vitro precision reflects the optimal reproducibility obtainable by the instrument. This is determined by the statistical error of the signal, the accuracy of detection of the bone edge and the reproducibility of the object positioning. Long-term *in vitro* precision is also affected by machine variations and drift. Both the Lunar and Hologic systems were very stable and the *in vitro* precision error for the spine was close to that expected from quantum statistics (Sorenson et al, 1988). *In vivo* precision is affected by the additional factors of subject repositioning and accurate relocation of areas of interest. In the present study, *in vivo* precision for spine measurements of normal and osteoporotic subjects was similar to previously reported figures obtained in young healthy subjects (Kelly et al, 1988; Pacifici et al, 1988; Wahner et al, 1988; Cullum et al, 1989; Mazess et al, 1989), although slightly worse in the femur than reported by Mazess et al (1989). Precision (coefficient of variation) of spine measurements is by definition a function of bone density and, therefore, worsens with decreasing bone density. However, in the femur this effect was less prominent and for the Lunar DPX measurements were not consistent. Of the three regions assessed in the femur, precision was consistently poorer in Ward's triangle than in the greater trochanter or the femoral neck. Precision for femur measurements tended to be less good for the Lunar DPX than the Hologic QDR-1000, probably because of the automatic selection of sites for measurement within the femoral neck by the former system.

An understanding of precision is crucial to the interpretation of bone density changes over a period of time and, hence, for monitoring the course of a disease or response to therapy. Bone density changes of 2–3% per year are thought to be clinically significant (Cullum et al, 1989). To be 95% confident that a BMD change has occurred, one must observe a BMD change of 2SD. For spine scans the precision error (SD) was about 0.01 g/cm^2 for both systems for non-obese subjects (Table V). Thus, for a spine BMD of 1.2 g/cm^2 or of 0.6 g/cm^2 we must observe a BMD change of 0.02 g/cm^2. This is a 1.7% change for the normal spine, but a 3.4% change in BMD for the osteoporotic spine. Thus, with present equipment and from two bone density measurements, we can only be 95% certain that 2–3% changes have occurred in non-obese subjects with high spine BMD.

Precision is also affected by the thickness of the subject. This deterioration in precision with body thickness is demonstrated by the phantom measurements at different depths of water (Table III); above 24 cm of water, precision is clearly worse for both systems. Most non-obese women have a body thickness in the range 20 cm to 25 cm at the level of the lumbar spine. By considering the proportion of body fat (Mazess et al, 1989) it has been estimated that a woman with a body thickness of 27 cm has a similar attenuation to 24 cm of water. Thus, many obese women fall within the range of measurements where precision is deteriorating.

Low BMD and increased body thickness exacerbate the problem of edge definition of the bone. Even using the slow scan speed, manual adjustment of the bone region was necessary on the Lunar DPX at all water depths above 22 cm and for low bone densities. Thus, the precision of the Lunar DPX is more likely to deteriorate when scanning osteoporotic and obese subjects than the precision of the Hologic QDR-1000.

Degenerative changes and extraskeletal calcification in the region of the lumbar spine will also affect long-term precision of both systems.

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Registration of MR and CT images for skull base surgery using point-like anatomical features

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Abstract. We have developed a registration technique for combining magnetic resonance imaging (MRI) and computed tomography (CT) images of the skull base for use in surgical planning. The technique is based on user identification of point-like landmarks visible in both modalities. The combination of images involves a small amount of expert interaction, is relatively quick and preliminary evaluation indicates that it is accurate to within 1.5 mm. Registered or fused images can be viewed either on an image processing workstation, or fused images can be printed onto conventional film for convenience in clinical use. We present one patient in order to demonstrate the technique's indications and advantages.

In skull base surgery, the information provided by magnetic resonance imaging (MRI) and X-ray computed tomography (CT) is complementary. The soft tissue pathology and nervous tissue are better visualized by MRI, while the bony structures of the temporal bone, including the middle ear, cochlea and internal auditory meatus, are better visualized by CT.

Patients undergoing skull base surgery at this institution have thin slice MRI and CT scans for surgical planning purposes. Conventionally these are printed onto films and displayed side by side on a light box using the expertise of the diagnostician or surgeon to mentally fuse the images. We consider this method of viewing the images to be suboptimal and, therefore, hypothesized that considerable benefit could be gained by combining both sets of data. There are two stages to achieving such a combined display. The first is to register the images to determine the geometric transformation relating the coordinate systems of the two 3D data sets, and the second involves fusing the images, by generating a single image from the two registered originals.

Various techniques have been proposed for registering images from different tomographic modalities. External markers attached to the patient's skin or to a thermoplastic face mask have been used to register nuclear medicine images to MR or CT images (Evans et al, 1988; Fleming, 1989; Wilson & Mountz, 1989; Hawkes et al, 1990; Meltzer et al, 1990; Rizzo et al, 1990). These methods do not provide sufficient accuracy for registering MR and CT to each other because of movement of the markers. Skin markers are most accurate when left in position for both scans, but this is inconvenient if not impossible when scans are performed on different days and/or at different institutions. Stereotactic frames have been used for registering MR images with CT images (Peters et al, 1986; Schad et al, 1987; Henri et al, 1989; Zhang et al, 1990), but the invasiveness of a stereotactic frame limits its use to stereotactic procedures and, in any case, stereotactic frames are often too large to fit in the head coils of MR scanners.

A more flexible approach to image combination is to use anatomical features visible in each modality rather than using external markers or frames to achieve registration. We propose that the use of anatomical features for registration has the potential for greater registration accuracy than external markers and requires less interference with normal radiographic procedures. Various anatomical features have been proposed for registering MR and CT images. The features can comprise points (Chen et al, 1985; Boesecke et al, 1990), centroids of segmented regions (Bartoo & Hanson, 1989) or surfaces (Gamboa-Aldeco et al, 1986; Pelizzari et al, 1989). Since slice planes will, in general, be different for the MR and CT images, it is essential that the registration is in 3D.

In our application only a small portion of the head is imaged (an axial distance of a few cm centred on the temporal bone). Pelizzari et al (1989) have reported using the skin surface to register MR, CT and positron emission tomography (PET) images, but unfortunately we have found that in our application the area of skin surface sampled by both imaging modalities is rather small and hence skin surface fitting is an ill posed problem. More fundamentally, the skin surface, especially around the ears and base of the skull, is distorted differently and non-reproducibly by the different head restraining devices used in MR and CT scanners. Like Chen and Boesecke (Chen et al, 1985; Boesecke et al, 1990) we use point landmarks to achieve registration. Three linearly independent 3D points are required to determine uniquely the 3D coordinate system of each imaging modality if voxel dimensions are known. However, we propose using a large number of points to improve registration reliability and accuracy, as Evans et al (1989) have reported for registering MR and PET data. The skull base region has several features visible on both MR and CT images, but the accuracy with which individual features can be located is not necessarily sufficient for registration. By using additional points and a least squares algorithm for registration, it is possible to achieve a registration accuracy greater than the accuracy with which each point is located, assuming the location error is random.

In this paper we present the application of this technique to one patient. The patient had an acoustic neuroma on the right side, which was surgically removed using a translabyrinthine approach.

Materials and methods

Acquisition

MR and CT images of the skull base are acquired on an outpatient basis at different institutions on different days. MR images are acquired with 256 × 256 pixels per slice, and a slice thickness of between 2 mm and 5 mm (Philips Gyroscan S15). The pulse sequence used is selected according to the normal clinical protocol. CT images are acquired with 512 × 512 pixels per slice and a slice thickness of between 1.5 mm and 3 mm (GE Medical Systems CT 9800). Plan views from the first set of images to be acquired can be used as an approximate aid to positioning the slices for the second modality. This is not essential for registration, but it helps ensure that the same volume of the patient is imaged in both modalities and it assists subsequent location of the point-like landmarks if the images from the different modalities are approximately co-planar. The images are transferred onto a network of SUN workstations for further processing. Each CT slice is translated anteriorly or posteriorly to correct for gantry angle and hence produce an orthogonal data set, but no distortion correction was necessary on the MR images. We have measured the geometric distortion of our MR scanner (Philips Gyroscan S15) to be a maximum voxel displacement of 2.3 mm for transverse slices at the periphery of the head coils field of view, with an average integral non-linearity of less than 0·8 mm (Price, 1990). This is within the registration accuracy required for our application.

Criteria for selection of point-like landmarks

The following are examples, but not an exhaustive list, of point-like structures which may be used for registration.

A point anatomical structure (*e.g.* the apical turn of the cochlea).

The intersection of two linear structures (*e.g.* blood vessel bifurcation or confluence).

A particular topographic feature on a surface (*e.g.* an identifiable part of a sulcus or gyrus).

The intersection of a surface structure with a linear structure (*e.g.* where a nerve passes through a foramen).

The intersection of three surface structures.

The 3D coordinate of each feature must be identified in each data set.

Registration

The unregistered MR and CT images are displayed as sequences of 2D slices on two SUN workstations placed side by side. Two workstations are used because a single SUN workstation does not allow a minimum of three slices from each modality to be displayed at full resolution (512 × 512 pixels per slice for CT). The user then identifies the 3D coordinates of equivalent point-like anatomical features in both modalities using a mouse and cursor. Careful scrutiny of the hard copy films of the images which are also displayed on a light box adjacent to the SUN workstation assists in this. The 3D coordinates of the selected points are used to determine the coordinate transformation relating the MR and CT images. This is achieved using a least squares fitting algorithm (Arun et al, 1987) which we have applied previously to external marker based registration of MR and single photon emission computed tomography (SPECT) images (Hawkes et al, 1990; Hill et al, 1990). Details of this algorithm are given in the appendix. The registration algorithm determines the three translations and three rotations of a rigid body transformation. The scaling (*i.e.* the voxel dimension for each modality) was determined by separate calibration as part of the routine quality assurance programme of each scanner, but could easily be determined from the location of the corresponding features. The registration algorithm calculates the registration error for each of the point landmarks and the root mean square (RMS) error for all points. The calculated registration transformation was used to transform the MR image data set to the coordinate system of the CT images using trilinear interpolation.

The study presented in this paper was on a 57-year-old woman with a suspected right acoustic neuroma, who had conventional MR and CT investigations as detailed in Table I. Six point-like anatomical structures were located in both modalities. These points are listed in Table II. Three independent observers located the six point-like landmarks in the MR image twice to give an indication of the precision of landmark location.

Display

The registered data set comprises an array of voxels, each of which contains two attributes: one from the CT

Table I. Image acquisition details

MR images
  Image dimensions 256 × 256 × 14
    Acquisition time 15 min with saddle head coil
    Voxel size 0.9 × 0.9 × 2.0 mm
    Post-gadolinium DTPA enhanced T_1-weighted spin-echo: echo time (TE) 30 ms, repetition time (TR) 450 ms

CT images
  Image dimensions 512 × 512 × 21
  Voxel size 0.48 × 0.48 × 1.5 mm
  No contrast

image, one from the MR image. Both these modalities provide information primarily on patient anatomy, so the colour overlay typically used to display images of anatomy (MR or CT) registered with images of function (SPECT or PET) (Hawkes et al, 1990) would tend to be confusing. To overcome this we have developed two alternative types of display. The first involves adjacent display of equivalent MR and CT slices selected from the registered image volume, with a linked cursor identifying equivalent regions in the two modalities. The second method involves generating a single grey scale distribution from the registered data volume by fusing the data with a logical operation at each voxel. For example we chose:

```
IF CT Hounsfield Number corresponds to bone
        DISPLAY CT attribute
ELSE
        DISPLAY MR attribute.
```

These fused images are printed onto film to enable them to be viewed on conventional light boxes.

Results

Accuracy

Each of the three independent observers were able to relocate the six anatomical features to within 1 pixel in each dimension of the MR image. This corresponds to a distance of 0.9 mm in the slice plane and 2 mm in the perpendicular direction.

The RMS registration error for the point-like landmarks is 1.43 mm. The registration accuracy will be better than this since a least square technique is used to derive the transformation matrix and, as more points are identified than are necessary to solve the transformation, there will be some averaging of errors.

Table II. Point like structures used to register MR and CT images

1) Tip of the alar cartilage (visible in both modalities).
2) The most inferior junction of the anterior wall of the sphenoid sinus with the sphenoid intersinus septum (visible in both modalities).
3) The modiolus of the left cochlea (visible in both modalities).
4) The modiolus of the right cochlea (visible in both modalities).
5) The termination of the naso-lacrimal duct in the maxillary sinus (visible in both modalities).
6) The confluence of the superior sagittal sinus and the transverse sinuses (visible in MRI) and the internal occipital protruberence (visible in CT).

Images

Figure 1 shows adjacent display of the MR and CT components of a single slice at the level of the internal auditory meatus taken from the registered image volume. Figure 2 shows the fused display of this same slice, with the CT value displayed in pixels where the Hounsfield number corresponds to bone and the MR value is displayed in the remaining pixels. Figure 3 shows this same fused display of a slice higher in the data set.

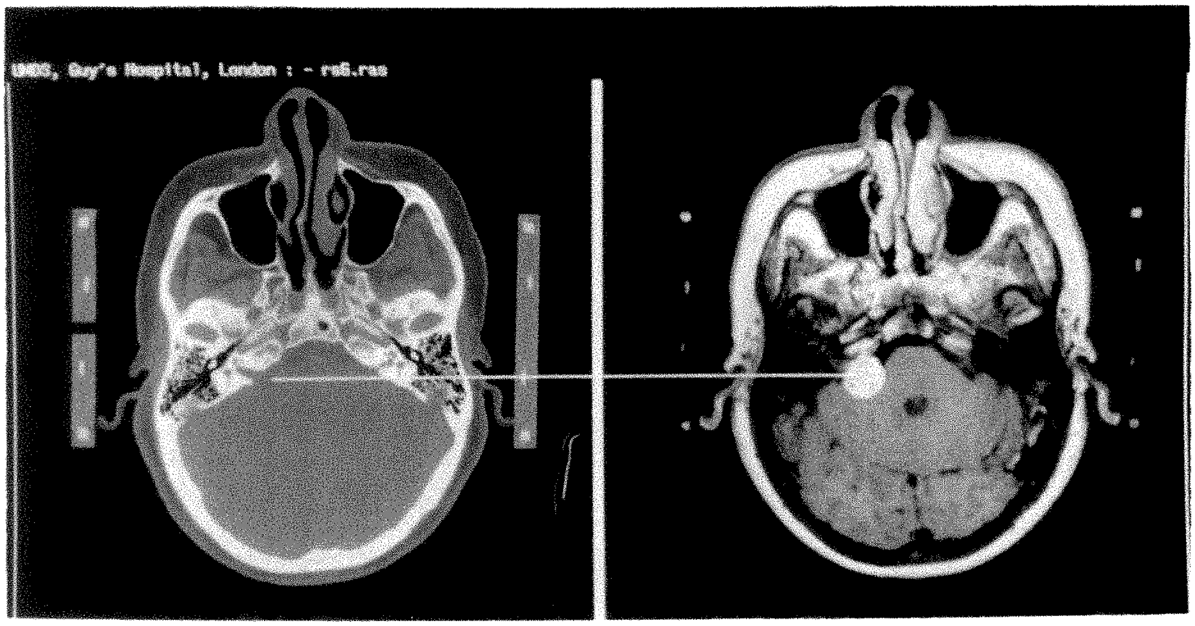

Figure 1. Adjacent display of a single slice at the level of the internal auditory meatus taken from registered MR and CT volume images. The linked cursor indicates the position in both modalities of the centre of an acoustic neuroma.

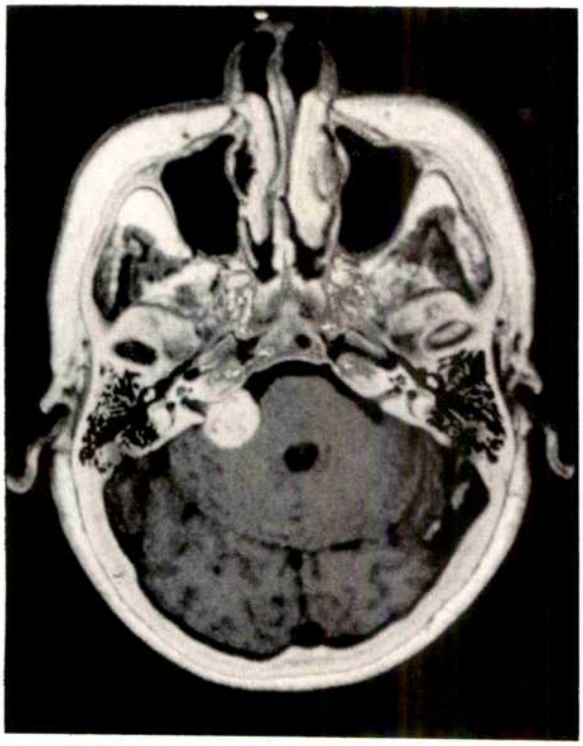

Figure 2. Single fused display of the MR and CT components of the images illustrated in Fig. 1. In the fused display, bone information from the CT image is displayed with soft tissue information from the MR image.

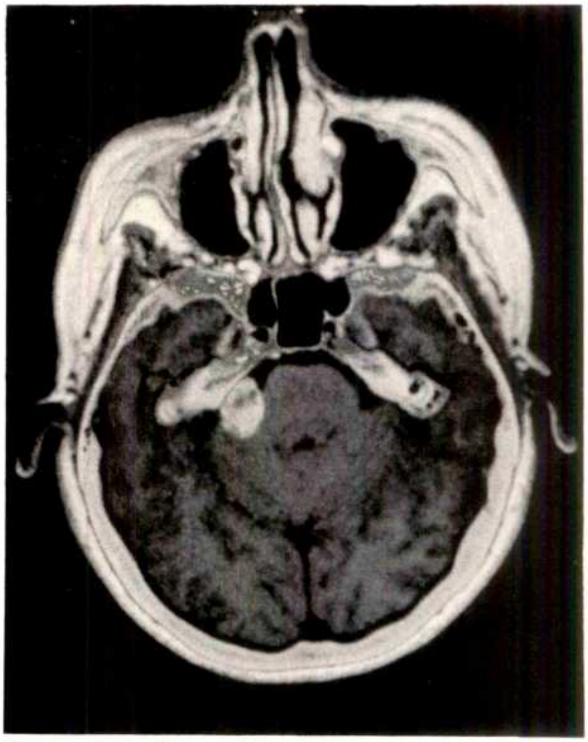

Figure 3. Fused display of a slice 9 mm more craniad than that shown in Fig. 2.

Discussion

We have developed a technique for registering MR and CT images which is entirely retrospective and does not interfere in any way with normal image acquisition. The technique requires a user, who is familiar with MR and CT appearances of the anatomy of the skull base, to identify between six and 12 point-like features. This process takes an experienced user less than half an hour. Once this is done, the calculation of the registration transformation and the interpolation of the image data takes a few minutes, but requires no user interaction.

The RMS and maximum error calculated by the registration program give an indication of the accuracy of registration. Only three points are required to determine the rigid body transformation of data from one modality to the other. We used six points and a "least squares" technique to calculate the best estimate of the transformation, which assumes that the errors on the location of each point is independent, random and approximately the same. The best points to choose for accurate calculation of the rigid body transformation would be around the periphery of the field of view. However, because the location error due to distortion in the MR image is highest at the periphery, it is more appropriate to select points evenly distributed around the site of interest.

As we have greater *a priori* confidence in the location of some of the features than others, it would be appropriate to use this *a priori* confidence to weight the least squares calculation. This is being implemented.

We have used a simple thresholding technique on the CT data to define bone in the fused images. Therefore, the partial volume effect will lead to aliasing in the final display, which becomes more severe with increasing CT and/or MR slice thickness. We are investigating the use of colour displays with appropriate look up tables to produce the most effective display.

For skull base surgery, registration and fused display clearly provide the surgeon and radiologist with better information on the precise geometric relationship between the soft tissue structures seen on MR and the bony structures seen on CT. Most lesions within the temporal bone are diagnosed by MR, *e.g.* acoustic neuromas and dermoids and cholesterol cysts. Nevertheless, CT is still required to establish the optimal surgical approach and to delineate the bony anatomy that will be encountered in a transtemporal resection.

The fused image can be displayed as a single grey level distribution and, therefore, can be printed onto conventional film using a laser imager or matrix camera. This is convenient, provides a familiar medium for display and enables the registered images to be used in the operating theatre.

In this paper, we have described the technique and presented results for a single patient. This technique has so far been applied to six patients with various skull base pathologies and the results of a full clinical evaluation of the method will be presented in due course.

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Appendix. Least squares fitting of two 3D point sets

The rigid body transformation relating two 3D image data sets can be determined by finding the least squares registration transformation relating an arbitrary number of approximately equivalent 3D points identified in the image data sets. To achieve this, we use an algorithm based on singular value decomposition (SVD) derived from Arun et al (1987).

The two 3D points sets $\{p_i\}$ and $\{p'_i\}$ are related by

$$p'_i = \mathbf{R}p_i + \mathbf{T} + \mathbf{N}_i \tag{1}$$

where each of p_i is a 3D point represented as a column vector, $\mathbf{R}$ is a 3D rotation matrix, $\mathbf{T}$ is a translation vector, and $\mathbf{N}_i$ is a noise vector arising as a result of errors in locating equivalent 3D points in the two image data sets.

Finding the registration transformation relating $\{p_i\}$ and $\{p'_i\}$ involves determining values of $\mathbf{R}$ and $\mathbf{T}$ which minimize

$$\Sigma^2 = \sum_{i=1}^{n} \|p'_i - (\mathbf{R}p_i + \mathbf{T})\|^2 \tag{2}$$

where n is the number of points in the point sets.

As described in Arun et al (1987), $\mathbf{R}$ and $\mathbf{T}$ can be decoupled by finding the centroids of each point set and subtracting these centroids from each point set to give $\{q_i\}$ and $\{q'_i\}$. In this way, the rotation transformation is the value of $\mathbf{R}$ which minimizes

$$\Sigma^2 = \sum_{i=1}^{n} \|q'_i - \mathbf{R}q_i\| \tag{3}$$

The matrix $\mathbf{R}$ can be calculated by first determining the matrix $\mathbf{M}$ given by

$$\mathbf{M} = \sum_{i=1}^{n} q_i q_i'^t \tag{4}$$

where the superscript t represents matrix transpose. Using SVD, the real matrix $\mathbf{M}$ can be decomposed into a column orthogonal matrix $\mathbf{U}$, a diagonal square matrix with non-negative entries $\mathbf{W}$, and the transpose of a square orthogonal matrix $\mathbf{V}$, such that $\mathbf{M}$ equals the product $\mathbf{UWV}^t$.

Provided the determinant of $(\mathbf{VU}^t)$ is $+1$, then

$$\mathbf{R} = \mathbf{VU}^t \tag{5}$$

If the determinant is -1, this solution is a reflection rather than a rotation. As the physics of the system constrains the transformation to be a rotation, the correct rotation can be found from

$$\mathbf{R} = \mathbf{V}'\mathbf{U}^t \tag{6}$$

where $\mathbf{V}'$ is obtained from $\mathbf{V}$ by setting the column corresponding to the most singular value of $\mathbf{M}$ to 0.

Having calculated $\mathbf{R}$, $\mathbf{T}$ can be found from

$$\mathbf{T} = p' - \mathbf{R}p \tag{7}$$

In our implementation, the SVD of $\mathbf{M}$ and matrix determinants were calculated using functions from the Numerical Recipes in C library (Press et al, 1988).

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Long term results of Cathetron high dose rate intracavitary radiotherapy in the treatment of carcinoma of the cervix

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Abstract. Between 1967 and 1974, 371 patients with carcinoma of the cervix have been treated by a combination of external beam radiotherapy and fractionated high dose rate brachytherapy using the Cathetron. A retrospective review was undertaken in 1986 and median follow-up time was 6 years. Life table analysis of survival and complications to 16 years was undertaken. International Federation of Gynaecology and Obstetrics (FIGO) stage distribution was 26%, 46% and 28% for Stages I, II and III, respectively, and 5 year survival was likewise 94% 63% and 37%. Age and histological type or grade were not found to influence survival. Recurrent disease was recorded in 142 patients; the first site was within the pelvis in 25% and as distant metastases in 17%. Following development of pelvic recurrence median survival was 28 weeks. Salvage surgery was performed in 32 patients, of whom five probably obtained survival benefit. Significant late morbidity was seen in a total of 71 patients (19%); in seven patients this was at more than one site. Late morbidity to the small bowel was recorded as Grade 2 in 10 patients and Grade 3 in 13; to the rectum, Grade 2 in 10 patients and Grade 3 in two patients; to the bladder, Grade 2 in 15 patients and to the vagina Grade 2 in 29 patients. Median time to onset for small bowel morbidity was 14 months, for rectum 18 months, for vagina 20 months and for bladder 52 months. 82% of all late morbidity had been seen by 5 years of follow-up, no case of late morbidity or recurrence was seen between 11 and 18 years of follow-up. These results are comparable to those reported for other methods in use at the time the patients were treated.

High dose rate (HDR) intracavitary therapy combined with external beam irradiation for the radical treatment of carcinoma of the cervix was established at South Wales Radiotherapy and Oncology Centre, Velindre Hospital, in November 1967. The method of treatment and early results of the first 144 patients were reported by Joslin et al (1972). This report deals with the long term results of treating all 371 consecutive patients from 1967 to 1974.

Method

The technique of treatment using the Cathetron machine in combination with external beam irradiation has been described previously, together with the dose escalation employed in the first 30 patients (Joslin et al, 1972). Briefly, intracavitary treatment was given once a week to a total of 4 fractions over 22 days. During this same period external beam megavoltage irradiation was give 4 days a week to a total of 12 fractions. External beam treatment was delivered by parallel opposed fields to the whole pelvis with a tapered central wedge designed to compensate for the fall off in dose lateral to the intracavitary sources. A summary of the radiation doses employed is shown in Table I. Selected patients with advanced disease received external irradiation without a central wedge for 1–2 weeks before commencing intracavitary treatment.

Patients have been regularly followed-up and these data were obtained from a retrospective review of the notes. Survival to cancer death and morbidity have been calculated using the logrank method.

Morbidity was assessed using the criteria of Crook et al (1987). Grade 1 morbidity consisted of mild symptoms requiring less than 6 months of medical management and without significant effect on functional status. Patients with Grade 2 moderate morbidity were debilitated by symptoms and fulfilled one or more of the following criteria: more than 6 months of medical treatment; in patient cystoscopy; hospitalization for treatment such as blood transfusion; non-fistulous rectal ulcers; stenosis of intestine or ureter deemed to be functionally significant. Also included in Grade 2 was functionally significant postcoital bleeding. Criteria for inclusion in Grade 3 severe morbidity included all fistulae (enterovaginal, enterocervical, vesicovaginal) and conditions requiring surgery or death. These criteria for moderate and severe categories are very similar to the Grades 3–4 in the system proposed by Chassagne (1980). As Crook et al (1987) comment it is the division between minor and moderate morbidity which remains somewhat subjective.

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Results

Patients

There were 371 consecutive patients with invasive carcinoma of the cervix whose median age was 54 years. 16 patients (4%) were less than 35 years old. International Federation of Gynaecology and Obstetrics (FIGO) stage distribution was 26%, 46% and 28% for Stages I, II and III, respectively. The histological type was recorded in 362 patients (98%) and was squamous cell carcinoma in 325 (90%) and adenocarcinoma in 37 (10%). Histological grade was recorded in 332 patients (92%), and was well or moderately differentiated in 71% of cases and poorly differentiated or anaplastic in 29% of cases. Median follow-up time was 6 years with a maximum of 18 years.

Survival

Survival to death from carcinoma of the cervix, sub-divided by stage, is shown in Figure 1. 5 year survival of patients with Stages I, II and III disease was 94%, 63% and 37%, respectively. Following development of pelvic recurrence median survival was 28 weeks.

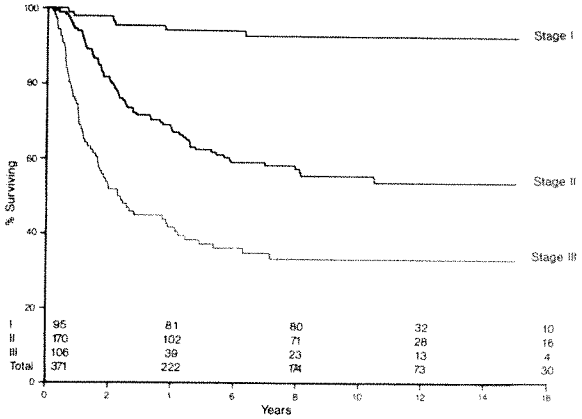

Figure 1. Actuarial survival following treatment for carcinoma of the cervix, sub-divided by FIGO stage. The number of patients remaining at risk at each 4 yearly period are also shown.

Patterns of recurrence

The incidence, by stage, of sites of recurrence is shown in Table II. Recurrent disease was recorded in a total of 142 patients. This appeared to be confined to the cervix in 55 instances; clinically this may be difficult to define and Table II also shows all pelvic recurrences, including cervical, parametrial and pelvic wall which was recorded as the only site of failure in 94 patients. Pelvic recurrence was associated with distant metastases

Table I. Radiotherapy dose prescription

Treatment modality	Manchester point 'A' dose	Manchester point 'B' dose	Maximum rectal dose
Cathetron 4 fractions	4 × 10 Gy = 40 Gy	4 × 2.75 Gy = 11 Gy	4 × 6 Gy = 24 Gy
External beam 12 fractions	12 × 2 Gy = 24 Gy	12 × 2.75 Gy = 33 Gy	12 × 1.66 Gy = 20 Gy
Total dose in 21 days	64 Gy	44 Gy	44 Gy
Cumulative radiation effect (CRE)	2412 reu	1479 reu	1580 reu

Table II. Sites of first recurrence

		Patients	Recurrence confined to cervix	Pelvic recurrence including cervix	Distant metastases	Both pelvic recurrence and distant metastates	Total patients with recurrence
Stage IB	*n*	95	3	4	3	0	7
	%		3	4	3	—	7
Stage II	*n*	170	23	43	34	6	71
	%		14	25	20	4	42
Stage III	*n*	106	29	47	27	10	64
	%		28	44	26	9	60
All patients	*n*	371	55 (15%)	94 (25%)	64 (17%)	16 (4%)	142 (38%)

The numbers of patients followed-up by year and, therefore, the length of follow-up on which these figures are based, are shown in Fig. 1.

(which includes para-aortic nodes) in 16 patients. Distant metastases without pelvic recurrence was seen in 48 patients. The tendency for recurrence to increase progressively with stage is also demonstrated in Table II. For example, recurrence within the cervix itself occurred in 3%, 14% and 28% of patients with Stages IB, II and III disease, respectively. A very similar trend is demonstrated for recurrence within the pelvis. However, the incidence of distant metastases was 3% in Stage IB, 20% in Stage II and 26% in Stage III. The similar rates seen in patients with Stages IIB and III disease may be caused by a greater proportion of patients with Stage III disease dying of pelvic recurrence before metastases had time to develop.

Table III shows the cumulative proportion of recurrences and morbidity occurring which is of interest in relation to deciding follow-up policy. It will be seen that metastases are rather slower to develop than pelvic recurrence and that by the end of 5 years 93% of pelvic recurrence, 86% of metastatic disease and 82% of Grades 2 and 3 late morbidity has already occurred. Five patients recurred between 7 and 11 years, when 185 out of the original total of 371 patients were still being followed-up. One patient with Stage I disease recurred locally. Out of two patients with Stage II disease one recurred locally and one with metastases, and of two patients with Stage III disease one recurred locally and one with metastatic disease. 87 patients were followed-up for between 11 and 18 years and no further recurrence or morbidity were recorded in this group.

Influence of age on survival

5 year survival was 69% in the 16 patients less than 35 years old compared with 63% in the older patients, a difference which is not significant ($p = 0.6$). Table IV shows all patients grouped by age and stage; logrank comparison of the survival rates within each stage was not significant ($p = 0.4$, 0.06, 0.4 for Stages IB, II and III, respectively).

Table IV. Survival by age group and stage

Age (years)	Stage IB		Stage II		Stage III	
	n	% 5 year survival	*n*	% 5 year survival	*n*	% 5 year survival
less than 40	15	93	12	50	7	43
40–49	25	100	40	48	32	27
50–59	32	94	52	76	32	40
more than 60	23	90	66	64	35	43
Total	95	94	170	63	106	37

Influence of histology on survival

5 year survival for squamous cell carcinomas was 63% compared with 68% for adenocarcinoma; the difference was not significant, $p = 0.8$. The 5 year survival for well and moderately differentiated squamous cell carcinomas was 65% and for poorly differentiated or anaplastic carcinomas it was 64% ($p = 0.5$). For the adenocarcinomas the corresponding figures were 67% and 43%, respectively ($p = 0.11$).

Surgery following irradiation

In five patients hysterectomy was performed following curtailment of radiotherapy owing to acute reactions. 27 patients were suspected of having residual or recurrent disease at up to 14 months from completion

Table III. Cumulative percentages of recurrent and Grade 2 and Grade 3 late morbid events related to number of years of follow-up

		Recurrence confined to cerivix	Pelvic recurrence including cervix	Distant metastases	Total patients with recurrence	Grades 2 and 3 late morbidity
1 year of follow-up	Stage I	33	50	33	43	
	II	57	51	12	35	
	III	59	66	30	54	
	All stages	56	59	20	44	30
2 years of follow-up	Stage I	33	50	66	57	
	II	74	77	44	62	
	III	69	79	66	78	
	All stages	69	77	55	69	59
5 years of follow-up	Stage I	66	75	66	71	
	II	83	91	85	90	
	III	93	96	89	92	
	All stages	87	93	86	90	82
18 years of follow-up	All stages	100	100	100	100	100

All figures are percentages. The numbers of patients within each stage on which these proportions are based are given in Table II.

of radiotherapy. They were considered operable and proceeded to a hysterectomy with or without lymphadenectomy at a median time of 3 months from completion of radiotherapy.

In this group of 32 patients, death from recurrent cancer was seen in none of the 11 patients with Stage IB disease, six of the 17 patients with Stage II disease and two of the four patients with Stage III disease. In 21 cases the hysterectomy specimen showed no evidence of malignancy, 20 had no further recurrence of cancer and one died from distant metastases, with no evidence of local failure. In 11 cases there was evidence of invasive carcinoma in the hysterectomy specimen, five remained free of disease, five died from further local recurrence and metastatic disease, and one patient died from metastatic disease with no further local recurrence. Therefore, only five patients of the total 32 may have obtained survival benefit from surgery. However, it is interesting to note that two of these were Stage II and two were Stage III cases, suggesting that radiotherapy may make some advanced cases operable and potentially curable. Although these five cases were salvaged by surgery they have been included in the analysis of survival as being treated by radiotherapy alone.

Early morbidity

The acute effects of the treatment protocol were described in the original publication (Joslin et al, 1972). In five patients radiotherapy was curtailed owing to acute radiation bowel reactions and hysterectomy with pelvic lymphadenectomy was performed. Radiotherapy was not completed in two patients with progressive uraemia and in two patients whose tumours continued to grow. These four patients died quickly from their disease, but have been included in the survival statistics.

Late morbidity

Only complications which developed at least 1 month after the completion of radiotherapy were considered late complications. While treatment failure manifests itself by detectable recurrent disease, late treatment morbidity is invariably underestimated because a number of patients do not survive long enough to suffer it. To overcome this, Figure 2 employs the life table method to show the incidence of late morbidity to small bowel, rectosigmoid, bladder and vagina in patients who remain "at risk" by virtue of being alive at each follow-up period. This period of time is determined partly by when they were treated and the length of follow-up, and partly by the course of their disease—whether they recurred early and died.

Figure 2 charts the incidence of Grades 2 and 3 late morbidity. Median times to presentation of late morbidity vary and were 14 months for small bowel, 18 months for rectosigmoid, 20 months for vagina and 52 months for bladder. The proportion of all late morbidity presenting by 1, 2 and 5 years of follow-up, respectively, was 30%, 59% and 82%. 22 out of a total of 35 small and large bowel events (63%) occurred in the first 2 years. There were no deaths attributed to late morbidity. If all patients had been discharged from follow-up after 7 years, seven cases of Grade 2 morbidity and one of Grade 3 morbidity would perhaps not have been seen immediately in the clinics.

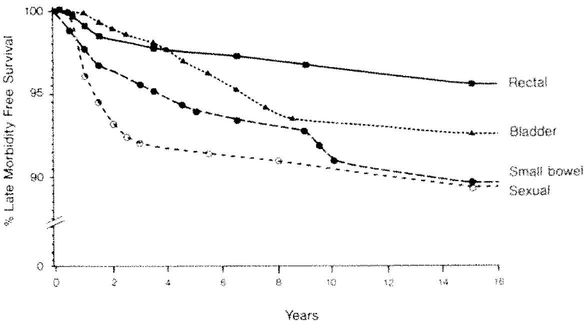

Figure 2. Life table showing the proportion of surviving patients remaining free of Grade 2 and Grade 3 late morbidity. The number of patients remaining at risk at each 4 yearly period are shown in Figure 1.

A total of 71 patients (19%) had some Grade 2 or Grade 3 morbidity. Seven patients had more than one site of significant morbidity; rectal bleeding was associated with vaginal bleeding in two cases, with haematuria in one case and with laparotomy for small bowel damage in one case. Vaginal bleeding was associated with Grade 3 small bowel damage in one case and haematuria in two cases.

a) Small bowel. Small bowel morbidity was recorded in 44 patients. Within Grade 1, 21 patients had one or more attacks of abdominal colic requiring no specific treatment in most cases; others required dietary advice or the use of antispasmodics. Within Grade 2, 10 patients required admission to hospital for investigation and treatment for subacute intestinal obstruction by nasogastric aspiration and intravenous fluids. Within Grade 3, 13 patients (4%) required surgery, 12 for treatment of intestinal obstruction due to strictures, most commonly at or near the terminal ileum, and in one patient for perforation of small bowel. In two patients, further surgery was required. The time to surgery was from 1 to 115 months (median 14 months). Nine of 13 patients treated by surgery had relief of symptoms but four patients continued to have intermittent attacks of abdominal colic.

b) Rectosigmoid. Within Grade 1 eight patients required short term treatment with steroid enemas. In Grade 2, 10 patients had one or more episodes of rectal bleeding requiring blood transfusion developing from between 4 and 13 months; the median was 18 months. Within Grade 3 two patients required surgery for stricture, one having resection, the other an end colostomy with oversewing of the distal lumen. There were no cases of recto vaginal fistula.

c) Bladder. In Grade 1 a total of 79 patients complained of one or more episodes of dysuria and increased frequency of micturition in the absence of urinary infection. In the majority of cases, the symptoms were transient but six patients had persistent symptoms. In Grade 2, 15 patients (4%) complained of one or more episodes of haematuria presenting between 14 and 107 months; the median was 52 months. Cystoscopy was carried out and the findings were either non-specific or of telangiectasia. In Grade 3 no patients required surgery for urinary complications and there were no proven cases of ureteric obstruction, except in the presence of local recurrence. However, it must be stated that routine post-treatment intravenous pyelograms were not done in asymptomatic patients.

d) Sexual. Within Grade 1 vaginal shortening or stenosis was noted in 93 cases (25%), usually an asymptomatic finding in elderly women. 14 patients (4%) complained of significant deep dyspareunia. This symptom was not part of the routine enquiry and further cases may not have been detected. In Grade 2, 29 patients (8%) complained of post-coital bleeding, at 7 to 101 months; the median was 14 months. The findings were non-specific or revealed telangiectasis and no specific treatment was required. Within Grade 3 there were no cases of fistulae not associated with local recurrence.

Discussion

HDR intracavitary afterloading for the treatment of patients with carcinoma of the cervix was started by O'Connell et al, in 1967. Radiation dose escalation studies were performed subsequently in a pre-operative setting (O'Connell et al, 1967), to allow pathological assessment of the acute effects and comparison with standard radium insertions to be made. From 1967 a standard treatment for HDR brachytherapy was established in Cardiff to treat patients with tumours larger than FIGO Stage IB, later to include patients with Stage IB tumours, using a central uterine tube and two ovoids together with external beam therapy using a central tapered wedge (Joslin et al, 1972). Treatment times were prescribed to give point A doses for an "average" patient, and were not modified for each individual treatment. This was necessary because the relative positions of the tube and ovoids were not fixed relative to each other, and because the treatment time of less than 5 min did not permit practicable dosimetry calculations. Analysis of treatments undertaken since has shown that point A doses defined from the intrauterine tube flange may vary from +56% to −47% (Joslin & Flynn, 1984). The ICRU report (1985) on dose specification for reporting intracavitary therapy in gynaecological cancer, which recommends defining a 60 Gy envelope to provide comparison of doses between centres, has proved difficult to apply retrospectively and none of our published studies of HDR intracavitary afterloading or the reports listed in Table VI have used this method of reporting. Table V shows published data from centres employing radical combinations of external beam with HDR intracavitary treatment for treatment of carcinoma of the cervix. The mean 5 year survival for patients with Stage I disease was 86% (range 100–71), for Stage II 66% (range 82–54) and for Stage III 46% (range 74–33). The 5 year survival results for our patients with Stages I, II and III disease of 94%, 63% and 37%, respectively, are close to these mean figures.

Table VI shows data reported from other centres on late morbidity following radiotherapy which includes HDR afterloading. There are a number of problems

Table V. Reports since 1980 of results from other centres of primary treatment of carcinoma of the cervix by radical radiotherapy including HDR remote afterloading but without planned surgery, giving 5 year survival figures subdivided by clinical stage

	Stage I		Stage II		Stage III	
	n	% 5 year survival	*n*	% 5 year survival	*n*	% 5 year survival
FIGO, 1987	160	77	358	58	386	38
Joslin, 1991	95	94	170	63	106	37
Arai et al, 1980	86	83	173	71	212	51
Rotte, 1980	42	83	59	75	11	37
Newman et al, 1983	92	81	A 53	74	92	27
			B 50	40		
Kuipers, 1984	21	76	54	74	36	36
Sato et al, 1984	8	97	31	55	44	57
Utley et al, 1984	29	89	50	58	43	33
Koga et al, 1987	14	85	20	68	43	51
Teshima et al, 1987	A 8	100	A 22	65	85	41
	B 22	86	B 53	72		
Akine et al, 1988			B 20	60	B 37	54
Cikaric, 1988	3	100	85	54	52	37
Ilic & Ristic, 1988	232	93	462	73	430	54
Mizoe et al, 1988	17	71	68	66	212	39
Vahrson & Romer, 1988	24	71	37	76	29	62
Shu-Mo et al, 1989	2	100	65	82	23	74
Total *n*/mean %	855	86%	1830	66%	1841	46%

Table VI. Complication rates reported by other centres using HDR remote afterloading brachytherapy for carcinoma of the cervix. Data is only included for patients treated exclusively by radiation, without surgery. Criteria for severity of complications were not standardized and are included in summarized form in the Table

Author	*n*	Criteria	Bladder		Rectum		Small bowel	
			n	%	*n*	%	*n*	%
Joslin, 1991	371	Crook Grade 2	15	4	10	3	10	3
		Grade 3	0		2	0.5	13	4
Rotte, 1980	112	Oedema or ulceration	1	0.9	3	3	NR	
Newman et al, 1983	291	Symptoms	11	4	2	0.7	11	4
		Surgery	1	0.3	4	1	9	3
Kuipers, 1988	142	Life threatening	5	4			9	6*
Sato et al, 1984	87	Requiring medical or surgical treatment	8	9	13	15	NR	
Utley et al, 1984	127	Outpatient treatment			32	25#		
		Fistula, transfusion, surgery			9	7		
Teshima et al, 1987	200	Kottmeier G2 and G3	6	3	14	7	4	2
Akine et al, 1988	84	Significant non-surgical	1	1	20	24	0	
		Surgical	0		3	4	0	
Cikaric, 1988	140	Inflammation/bleeding	6	4	6	4	NR	
		Fistula	1	0.7	4	3	NR	
Ilic & Ristic, 1988	1158	Mild transient			232	20^{+}		
		Moderate objective			81	7		
		Fistula, surgery			40	4		
		Death			3	0.2		
Mizoe et al, 1988	206	Mild	NR		24	12	NR	
		Significant non-surgical	7	3	3	1	NR	
		Surgical	1	0.5	3	1	NR	
Himmelmann et al, 1985	107	Regraded Kottmeier G1	3	3	1	1	0	
		G2	0		0		0	
		G3	0		0		0	
Shigematsu et al, 1983	143	Non-surgical	3	2	51	36	3	2
		Surgical	0		0		0	
Glaser, 1988	1131	Regraded Kottmeier G2	4	0.4	7	0.6	NR	
		G3	1	0.1	2	0.2		
Uzel et al, 1988	459	Kottmeier G2	28	6			73	16*
		G3	6	1			23	5
Alberti & Busch, 1988	113	Regraded Crook, G2	8	7	29	26	NR	
		G3	5	4	5	4		
Shu-Mo et al, 1989	380	Symptoms only	27	7	51	13	NR	
		Moderate objective	NR		45	12	NR	
		Marked constriction perforation	NR		6	2	NR	
Koga et al, 1987	60	Kottmeier G1	0		7	12	NR	
		G2	0		2	3	NR	
		G3	2	3	4	7	2	3

*Large and small bowel.
#Late complications reported together but "virtually all rectal".
$^{+}$Late complications all reported together.
NR = not recorded.

when comparing reported results of which the most important is the amount of variability employed in defining the grades of morbidity. Sismondi et al (1989) have examined this variability in detail in a review of 96 articles from which 22 different classifications emerged, and in only eight instances had the classification been published previously. Following the early classification of Kottmeier and Gray (1961) a more systematic approach to reporting complications was introduced by Chassagne in 1980 but alternative systems have continued to appear (Perez et al, 1984; Crook et al, 1987; Dische, 1988; Rubin, 1988). We decided to use the system of Crook because it can be applied simply to retrospective data. A further problem is the method of statistical presentation, which commonly states only the overall number of complications seen. The actuarial, or life table method, as used here, indicates the incidence of complications in relation to the number of patients remaining alive and at risk. This enables a comparison of the risk of morbidity at a particular time to be made. An important question requiring further study is the extent to which complications change with the passage of time. Retrospective analysis of our data has not allowed us to report adequately on this and the application of prospectively agreed grading criteria for each system at risk would permit a better analysis.

The question of whether to carry out radical surgery following radical radiotherapy can be difficult, especially if the tumour was originally at an advanced stage. Only five of the 32 patients operated on in this series were felt to have benefited from surgery. Experience since these patients were treated has shown that many cervical biopsies, reported as showing viable carcinoma at the time of the final intracavitary treatment, do not always progress to subsequent recurrent tumour. In the few patients whose general condition, initial staging and degree of tumour regression could make them candidates for radical surgery, it is our present practice to repeat biopsy at 1, 2 and 3 months and to consider surgical salvage only if biopsy at 3 months remains positive.

An indication of the worth of long term follow-up can be gained from Table III which shows that 80–90% of all recurrence and morbidity had manifested by 5 years of follow-up. Beyond 7 years, when 185 patients were still attending, we detected five patients with recurrent disease and seven with late morbidity. Whether follow-up beyond 7 years could be regarded as cost effective, and whether the local re-referral arrangements would have brought these cases to our attention had they been discharged, we cannot tell. These patients make a contribution to the overall outcome analysis and support arguments for continued follow-up in an academic setting. No case of recurrence or morbidity has been seen in 87 patients followed for between 11 and 18 years, and no case of in-field second primary tumour has been seen.

In conclusion, we consider the treatment technique used and the results achieved gave survival and late complication rates comparable to those reported for the other methods in use at the time.

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Treating the vaginal vault in carcinoma of the endometrium using the Buchler afterloading system

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Abstract. The advent of high-dose-rate afterloading intracavitary radiotherapy has implications for both staff safety and the possibility of convenient, outpatient-based treatment for the patient. We have carried out a retrospective analysis of its use with high-activity iridium 192 and the Buchler machine to treat the vaginal vault in patients with adenocarcinoma of the endometrium, most of whom also received external-beam radiotherapy to the pelvis. We have compared the survival, complication and local control rates with a comparable group of historical controls treated with low-dose-rate intracavitary caesium ovoids. Complication rates, which included vaginal stenosis not volunteered by the patient, were 16% (95% confidence intervals 6–26%) in the study group and 28% (95% confidence intervals 17–41%) in the control group, with no serious complications requiring surgery. The actuarial survival was 92% at 5 years in the study group, and 94% at 5 years in the control group. Local control was 94% at 5 years in the control group and 98% at 5 years in the study group. The authors suggest that the use of high-dose-rate intracavitary radiotherapy, with the Buchler afterloading system, for vaginal vault irradiation in carcinoma of the endometrium is a convenient, safe and quick method, which does not necessitate admission or sedation of the patient. In addition it provides complete radiation protection for staff.

The Buchler high-dose-rate afterloading machine was installed at Hammersmith Hospital in October 1983 and has been used virtually exclusively from February 1984. It has the advantage, in comparison with intermediate dose-rate therapy, of a shorter treatment time, which does not necessitate long periods of isolation for the patient (Vaeth et al, 1988). Previous experience with afterloading techniques in gynaecological malignancy of higher dose-rate than radium sources, which were used historically, has identified an increased complication rate (Wilkinson et al, 1980). On this basis an empirical dose reduction of 40% was selective for patients receiving high-dose-rate therapy. We analysed our study and control group, primarily with respect to complication rates, to establish whether the dose reduction arrived at produced a lower complication rate and, if so, whether this was at the expense of local control.

Patients and methods

Patients with low-risk histology (Stage I, Grade I) and only superficial myometrial invasion received intracavitary radiotherapy to the vaginal vault only; all other patients (Stage I, Grades II or III and Stage II disease) received external-beam radiotherapy post-operatively followed by intracavitary treatment.

In the study group we have assessed those patients with Stage I and II disease treated by high-dose-rate intracavitary therapy, with iridium 192, from October 1983 until January 1987 with a mean follow-up period of 3.8 years and a minimum period of 1 year. There were 50 suitable patients who satisfied the exclusion criteria detailed below.

The historical control group were those patients who received intracavitary radiotherapy, using ovoids containing caesium 137, to the vaginal vault between January 1980 and February 1984. There were 52 patients who had a mean follow-up period of 5.8 years and a minimum period of 1 year.

The patients in both groups were under the care of one consultant (H.E.L.). External-beam therapy was delivered with either a 6 MV Varian or an 8 MV Phillips linear accelerator. The external-beam field encompassed the true pelvis, with a margin to include iliac nodes, extending to the top of L5 with the corners blocked, using a three-field planned technique. The dose was 40 Gy or 45 Gy, depending on depth of myometrial invasion (Table I), using no more than 1.8 Gy per fraction. The intracavitary dose was prescribed at the surface of the obturator or ovoid. A dose reduction of 40% was selected for patients receiving high-dose-rate therapy, a compromise figure arrived at on the basis of previous experience (Dean et al, 1988; Joslin & Smith, 1971; Morita & Uchiyama, 1988) and current radiobiological knowledge. Hence the total dose was reduced to 15 Gy or 18 Gy, using high-dose-rate therapy, from 25 Gy or 30 Gy, respectively, using low-dose-rate therapy. High-dose-rate treatment was given in three

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Table I. Dose prescribed to each group, both external beam and intracavitary

	External beam	Intracavitary	
Superficial myometrial invasion (Grade I)	No external beam	O B	60 Gy × 1 6 × 6 Gy
Superficial myometrial invasion (Grade II or III)	40 Gy in 22F over 4.5 weeks	O B	30 Gy × 1 3 × 6 Gy
Myometrium invaded from halfway (all grades)	45 Gy in 25F over 5 weeks	O B	25 Gy × 1 3 × 5 Gy
Disease spread to uterine cervix (all grades)	45 Gy in 25F over 5 weeks	O B	25 Gy × 1 3 × 5 Gy

O = ovoids containing caesium 137; B = vaginal obturator containing iridium 192.

weekly fractions, commencing the week after external-beam therapy, or in six twice-weekly fractions in patients not receiving external-beam therapy. In the control group a single caesium insertion was performed after the same interval.

Exclusion criteria

1. Follow-up less than 1 year.
2. Inadequate surgery: less than total abdominal hysterectomy or radical hysterectomy.
3. Other malignant disease at the time of presentation.
4. Stage III or IV disease.
5. Histology other than adenocarcinoma.

Patients were analysed retrospectively with respect to complications (mild, moderate or severe), survival and recurrence rates. The two groups were comparable with respect to histology, age and distribution of disease stage. The patients in the study and control groups were of mean age 63.3 and 62.0 years, respectively (range 44–78 years and 43–83 years, respectively). In study and control groups, respectively, 34 and 35 patients had FIGO Stage Ib disease (invasion less than or equal to halfway through the myometrium); 13 and 14 patients had Stage Ic disease (myometrial invasion more than halfway) and three patients in each group had FIGO Stage II disease (FIGO, 1990). The mean follow-up period was 3.8 years in the study group and 5.8 years in the control group. Patients in both groups had completed external-beam therapy within the 2 weeks prior to intracavitary treatment.

Study group: high-dose-rate therapy

The entire procedure involving the high-dose-rate treatment is carried out as an outpatient. No sedation is required. On the first insertion the patient is placed in lithotomy position. Under sterile conditions the patient is examined, the length and breadth of the vagina measured and an appropriately sized obturator selected. Rectal and bladder dosemeters are inserted for the duration of the first treatment. The position of the dosemeters relative to the iridium source is verified by means of a pelvic radiograph and any necessary adjustment decided on with the physicists. The accepted upper limit for the rectal and bladder dose is 60% of the dose prescribed and the machine automatically cuts out if this dose is attained during treatment. In practice this did not occur in these patients.

Control group: low-dose-rate therapy

The historical control group were admitted to hospital the day prior to treatment and under general anaesthetic an examination was carried out followed by insertion of two suitably sized caesium ovoids to the vaginal vault. Once the required dose had been administered, the ovoids were removed by the nursing staff with premedication if necessary. The duration of inpatient stay was usually 4 days.

Statistics

An actuarial analysis of the survival to 5 years was calculated using the log-rank test (Peto et al, 1977) (see Fig. 1).

Dosimetry

The Buchler machine operates by means of an oscillating iridium-192 radiation source inside a stainless steel applicator. The oscillation is controlled by a rotating shaped programme disc driving a spindle attached to the source through a long cable and a gear mechanism. As the radius of the disc changes the source moves up and down the applicator. The shape of the disc determines the actual equivalent continuous source length. For all the patients in this group the equivalent source length was 3.5 cm. A Perspex obturator is fitted over the source applicator (see Fig. 2). It is shaped to

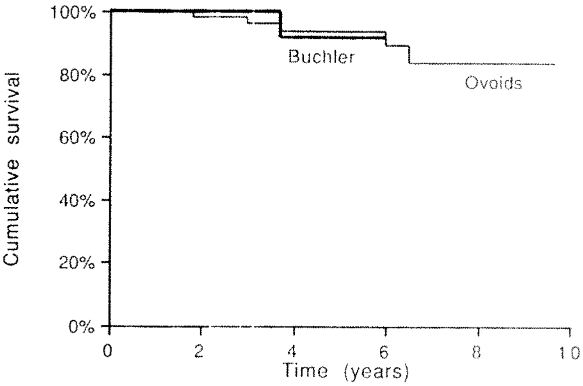

Figure 1. Life-table. Survival, with six deaths due to disease overall, was virtually the same in both groups. No statistical significance was found between the two groups. Actuarial analysis of survival was calculated using the log-rank test (Peto et al, 1977).

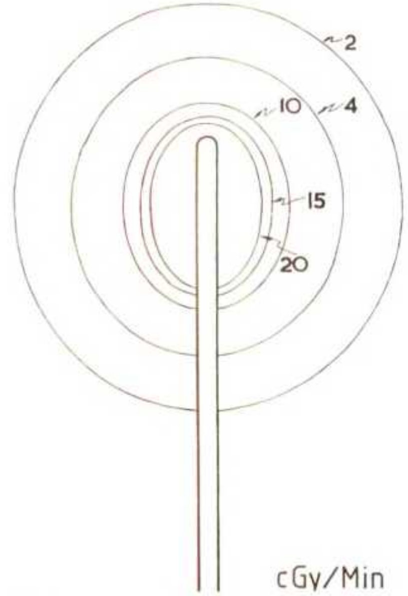

Figure 2. Isodose curve for source applicator in Buchler machine.

follow the isodose pattern so that the dose-rate over most of the surface of the obturator is uniform.

Two different diameter obturators are used, 2.5 cm and 3.0 cm, giving rise to a surface dose-rate of 30 and 23.5 cGy/min/Ci, respectively. The iridium-192 source, due to its relatively short half-life, is changed three times a year and during use its activity ranges from 10 Ci to 3.0 Ci. The treatment time per fraction consequently ranges from about 2.0 min to about 8 min depending on the source activity and the size of the obturator used. The obturator was designed by the departmental physicists to obtain an even isodose distribution to the whole vaginal vault (see Fig. 3). The dose-rate using the vaginal ovoids is approximately 60 cGy/h/Ci depending on the combination of sizes and configuration of ovoids used. The Buchler machine is illustrated in Fig. 4.

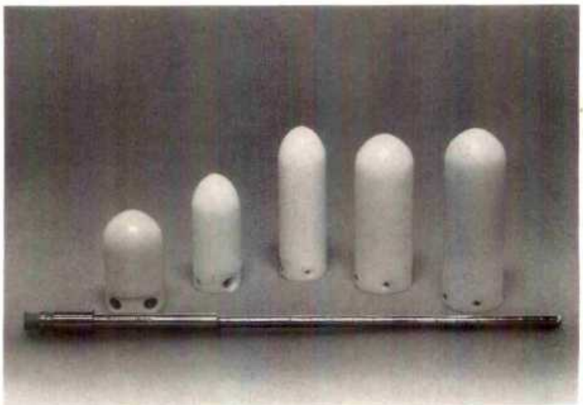

Figure 3. Obturators of different widths and lengths for use in treating endometrial carcinoma.

Follow-up

Patients were reviewed every 3 months for the first 2 years and every 6 months thereafter. Complications were noted and are detailed in Table II.

Results

The cumulative survival (Fig. 1) was 92% at 5 years in the study group, and 94% at 5 years in the control group. In the control group there were four local recurrences; one patient responded to further external-beam radiotherapy, one patient developed pulmonary metastases and one patient developed carcinoma of the vagina in her 10th year of follow-up. In the study group there was one local recurrence after 4 years and one

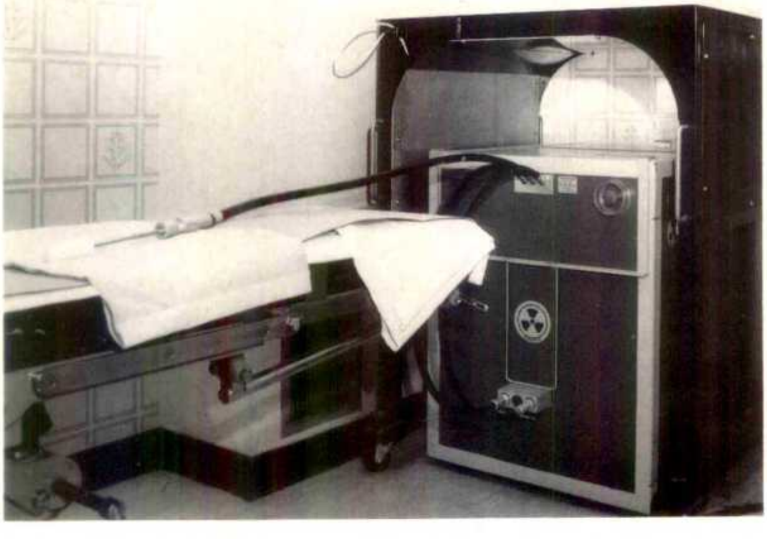

Figure 4. Buchler machine with channel and obturator for the treatment of endometrial cancer.

Table II. Complications in the two groups

	Control	Buchler
Total (including vaginal stenosis)	15/52	8/50
Intracavitary alone	2/21	1/15
Intracavitary and external beam	13/31	7/35
Complications apart from vaginal stenosis		
Mild complications	2	2
Severe complications	0	0

NB. No deaths due to complications. Mild complications: urinary frequency, diarrhoea and dysuria not requiring operative intervention.
Severe complications: those requiring further surgery.

patient developed a bony metastasis after 1 year. In addition, one patient in the study group and two patients in the control group developed other malignancies (carcinoma of the breast, Dukes B carcinoma of the colon and myeloma after 3, 4 and 6 years, respectively).

Overall complication rates include mild vaginal stenosis noted at follow-up, not necessarily volunteered by the patient. The complication rates of the two groups are not statistically significantly different. Ninety-five per cent confidence intervals for complication rates in the study group are 6–26%, and in the control group 17–41%.

From the above data there was no evidence to suggest that the greatly increase dose-rate for the intracavitary treatment gave rise to an increased recurrence rate. Similarly the dose reduction of 40% for intracavitary radiotherapy did not lead to an increase in local recurrence but it has to be accepted that this might be due to the external-beam radiotherapy that most patients received.

Discussion

The prognosis of Stage I and II endometrical carcinoma is good, with a 5-year survival of between 70 and 93% according to stage and grade (Spanos et al, 1978; Yeoh & Spittle, 1986; Pourquier et al, 1988; Vaeth et al, 1988; Ahmed et al, 1989; Sorbe et al, 1989). The overall survival of 92% at 5 years in the study group and 94% at 5 years in the control group compares favourably with the above series of endometrial carcinoma patients. Complication rates were also comparable to other series (Vaeth et al, 1988; Sorbe et al, 1989) with no patient requiring surgery and nobody dying as a result of a complication.

The need for post-operative external-beam radiotherapy in patients with Grade I and II superficial myometrial invasion is not yet resolved since many studies have failed to show a difference in outcome in treated and untreated groups (Onsrud et al, 1976; Salazar et al, 1978). In our practice, to prevent recurrence at the vaginal vault, those patients with superficial myometrial invasion and Grade I disease received intracavitary radiotherapy alone. Those with Stage Ib, Grade II and III disease received external-beam radiotherapy in addition.

Intracavitary treatment for gynaecological malignancies has been carried out since radium was first discovered. Its main disadvantage is radiation exposure to staff and other patients. This hazard is removed if remote afterloading systems are used. Traditionally, intracavitary radiation is given over many hours but the Buchler remote afterloading machine using a high-activity cobalt source enables such treatments to be given in minutes.

Changing from a low dose-rate (LDR) to high dose-rate (HDR) requires a modification dose to achieve the same radiobiological effect. To calculate the change in dose needed when treating with a high dose-rate, Liversage derived a mathematical relationship for determining HDR fractionated regimes that should be biologically equivalent to the previously used (LDR) radium therapy (Liversage, 1969). If a protracted LDR treatment lasting T hours is to be replaced by an HDR regime of N fractions, for large values of T this equation simplifies to $N \sim T/4$ (Dale 1990). Using this formula a 48 h LDR treatment replaced by high-dose-rate intracavitary radiotherapy would involve 12 individual fractions—not a practical possibility. Joslin and Smith (1970) suggested that when giving a single high-dose-rate treatment with the Cathetron (dose-rate 0.3–4 Gy/min), as opposed to a single treatment using radium over 24 h (dose-rate 0.01–0.03 Gy/min), there was an increased effect of about 60% with the former. A dose reduction of 40% was selected for our patients receiving HDR therapy. This is similar to that used by O'Connell et al (1967) and Morita and Uchiyama (1988). Dean et al (1988) used a dose reduction of 20%.

The advantages of a remote afterloading technique are logistic and economic. They include patient convenience, the avoidance of inpatient stay, sedation, reduced treatment time and better dosimetry with fixed obturators maintaining source position. Our results suggest that the use of high-dose-rate intracavitary therapy with a dose reduction of 40% compared with conventional low-dose-rate therapy does not alter complication rates. There is also no evidence that survival or recurrence rate are affected but follow-up for the HDR group does not extend beyond 6 years.

We conclude from this study that the use of high-dose-rate intracavitary radiotherapy for vaginal vault irradiation in carcinoma of the endometrium is a convenient, safe and quick method As awareness of the importance of avoiding unnecessary radiation exposure to staff increases, this form of treatment and its advantages should be taken into consideration by departments contemplating installation of an afterloading system.

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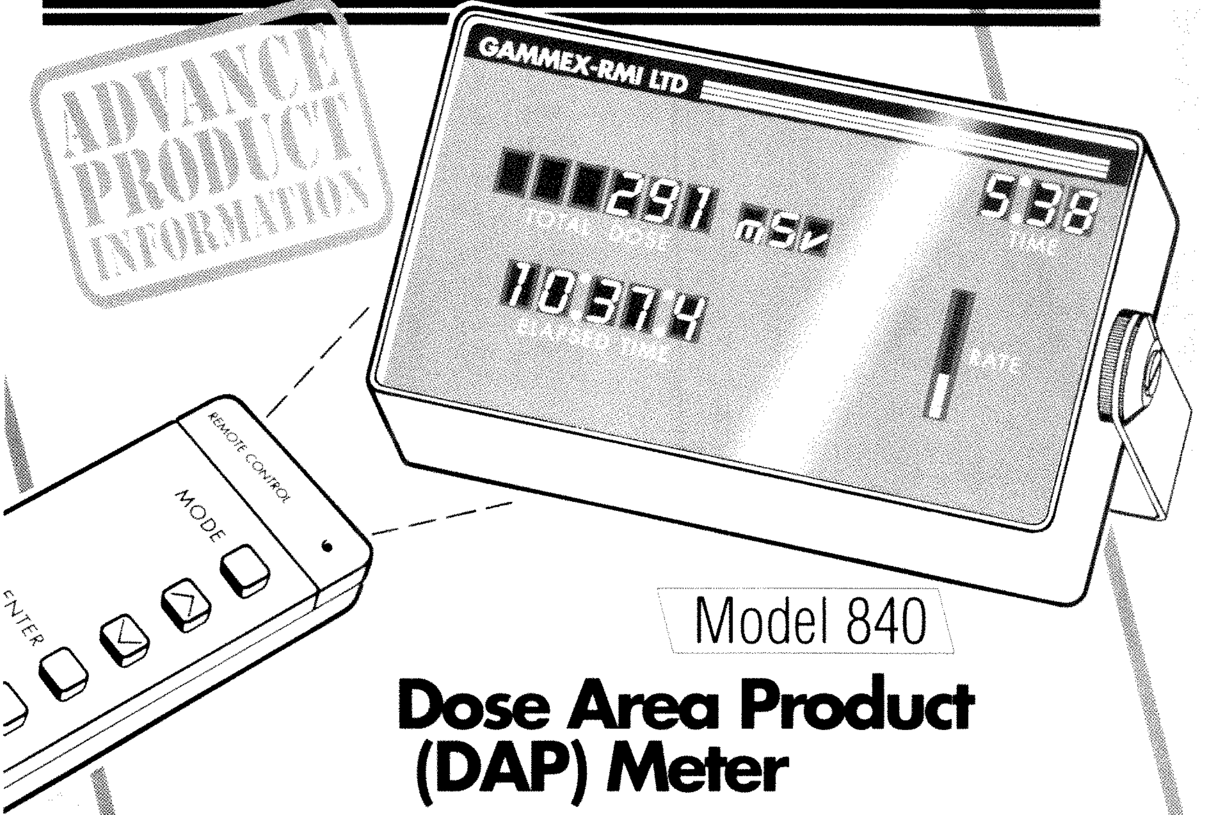

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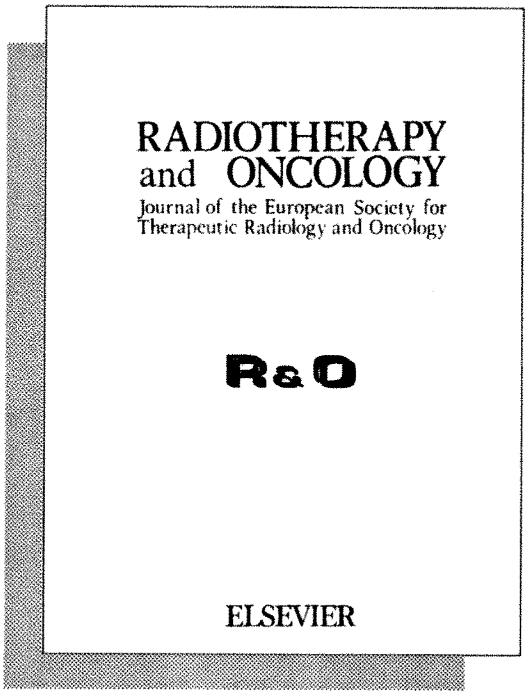

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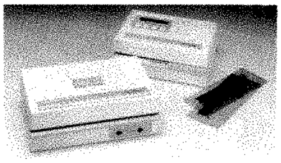

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A phantom for the measurement of contrast detail performance in film-screen mammography

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Abstract. A National Breast Cancer Screening Programme, based on X-ray mammography, has been introduced in the UK. The success of this screening programme is dependent on the production of high quality radiographs. There are various methods of assessing imaging performance in mammography, but contrast detail detectability measurements have an advantage in that the observation of radiographs is taken into consideration. The design and construction of a contrast detail phantom for the assessment of image quality in mammography is described. This phantom can be used to assess the imaging performance of mammographic film-screen combinations. The results of some measurements to verify the accuracy of the contrast predictions are presented together with some initial results of an investigation into the contrast detail performance of film-screen combinations used in mammography.

Breast cancer kills more women in the UK than any other form of cancer (Forrest, 1986). A National Breast Cancer Screening Programme, based on X-ray mammography, has been introduced in the UK. At present, it is considered that the main means of substantially reducing the number of deaths due to breast cancer is to detect the disease before the patient presents with symptoms.

The success of the National Breast Screening Programme is dependent on the production of high quality mammograms (Forrest, 1986). Film-screen mammography is perhaps one of the most technically demanding radiographic examinations, mainly caused by the composition of breast tissue and the nature of clinically significant objects. Therefore, it is important that film-screen combinations with good image quality are used in the screening programme.

Contrast detail detection measurements are a well established technique for assessing the performance of imaging systems (Cohen et al, 1984; Faulkner & Moores, 1986; Cowen et al, 1987). In a contrast detail experiment observers are shown images of circular discs that vary in both diameter and contrast. The observers are then asked to record the number of discs of a given diameter which they can perceive. The results are plotted on a contrast detail diagram. This paper describes the design and construction of a contrast detail phantom specifically for the assessment of the imaging performance of mammographic film-screen combinations. The contrast of the various circular objects in the test object can be estimated accurately given a knowledge of the peak tube potential and the generator waveform.

Theoretical contrast prediction

Owing to the difficulties of modelling X-ray photon interactions with matter in conditions of scatter, the model was restricted to the linear, scatter free situation. In this case the basic interaction is described as:

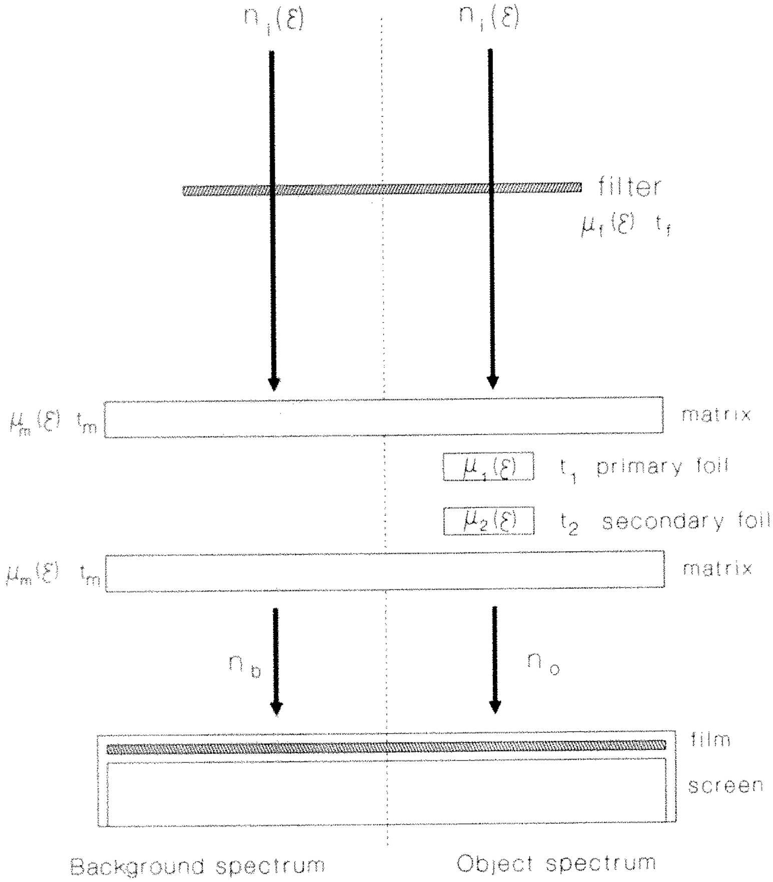
$$n(\varepsilon) = n_i(\varepsilon)e^{-\mu(\varepsilon)t} \qquad (1)$$

where $n_i(\varepsilon)$ is the number of photons of energy ε incident on a material of linear attenuation coefficient $\mu(\varepsilon)$ and thickness t, and $n(\varepsilon)$ is the number of those photons transmitted by the material.

Theoretical X-ray spectra were obtained using a computer program developed by Birch et al (1979). Spectra for both tungsten and molybdenum target X-ray tubes may be generated using this program. Constant potential X-ray spectra for molybdenum tubes were calculated using his program. The spectra are given in energy intervals of 0.5 keV and are normalized so that the sum of the photons in each spectrum is 10^5. The program user is required to specify the peak tube potential and any filtration that may be present.

Although some mammography sets operate using what is effectively a constant potential, others exhibit ripple in the tube potential waveform. To generate spectra with ripple it was necessary to modify the program to calculate the numbers of photons in energy intervals of 0.1 keV. 11 values were taken at equal time intervals on the tube potential waveform produced by a three-phase, six-pulse generator. Constant potential spectra were generated for each of these tube potentials. These were then summed to produce the final spectrum with the effects of ripple included. It may be noted that the ripple has the effect of softening the beam in comparison with a constant potential waveform generator at the same tube potential, that is, the effective energy of the spectrum is reduced.

Address reprint requests to K. Faulkner.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$\mu_m(\varepsilon)$ t_m
matrix
n_b
n_o
film
screen
Background spectrum
Object spectrum

Figure 1. Physical situation simulated by the contrast prediction program.

The Birch and Marshall program can also be used to calculate the energy-dependent mass attenuation coefficients for different elements and compounds (again, in energy intervals of 0.5 keV), based on data from the *Compilation of X-ray Cross-Sections* (McMaster et al, 1969). The interaction of the X-ray beam with an object is simulated by considering each energy interval separately and applying Eqn 1. In this way the transmitted number of photons of each energy is calculated to give the modified spectrum.

The situation modelled in the contrast prediction program is shown in Fig. 1. The model allows for various configurations of filter, test object medium (*i.e.* Perspex plates), attenuating foils, film-screen combinations, and input X-ray spectra. The use of two different materials to make up discs in the test object was necessary to obtain the fine differences in contrast. The incident beam is considered to have two components; (a) the "background component" is that part of the radiation beam being attenuated by the filter and test object medium only, and (b) the "object component" being the radiation which is attenuated by the foils inside the test object as well as the filter and test object medium (Fig. 1). Modifications to the component spectra are calculated as they pass through each attenuating stage. This results in two different spectra (the background and object spectra) from which the input radiation contrast to the film-screen system can be calculated.

The characteristic curve of a screen-film system for any particular X-ray spectrum depends in a complex way upon the light produced in the screen by the X-ray spectrum, the mechanisms by which the light is transmitted to the film, the interaction of the light with the film emulsion and the chemical processing of the film. Vyborny et al (1980a) proposed a simple solution to this problem by assuming that the system can be described by a single, modified characteristic curve. According to this approach the density on the film would be a function of a total effective exposure X, which is some linear combination of the contributions from X-rays of all energies. In other words, the X-ray fluence at each energy is to be weighted by a measure of the sensitivity of the system to X-rays of different energies, thus:

$$x = \int S(E)\phi(E)\mathrm{d}E \qquad (2)$$

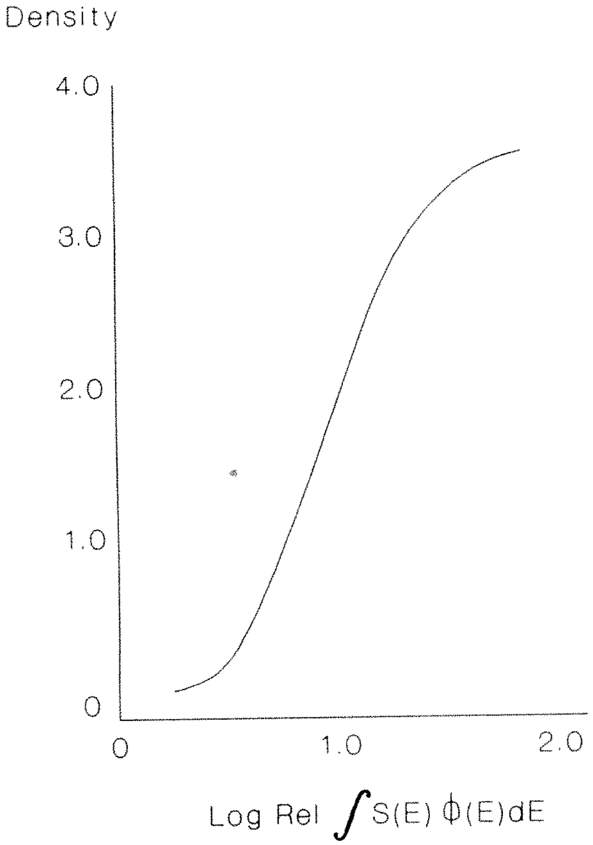


Figure 2. Characteristic curve adapted for the prediction of radiographic and object contrasts in screen-film systems.

where $S(E)$ is the system sensitivity function and $\phi(E)$ describes the incident X-ray fluence. In this way the sensitometry is reduced to a single curve still dependent on processing conditions (Fig. 2).

In the usual form of the characteristic curve, optical density is plotted against air kerma, or relative exposure to radiation or light, on a logarithmic scale. For a given X-ray spectrum, the air kerma may be deduced by multiplying the number of photons at a given energy by a photon to kerma conversion factor at that energy (Birch et al, 1979). This process is repeated for all photon energies, the air kerma being given by the summation over all energies. The difference between the conventional characteristic curve and the modifed one illustrated in Figure 2, is that the latter is modified by the system sensitivity function $S(E)$, defined as:

$$S(E) = [\phi_{1.0}(E)]^{-1} \qquad (3)$$

that is, the inverse of the X-ray fluence required to give a density of 1.0. Vyborny et al (1980a) defined contrast as:

$$C_{ob} = \{X_b - X_o\}/X_b \qquad (4)$$

in which C_{ob} is referred to as the object contrast, where X_b and X_o are the background and object effective exposures. Object contrast, as defined by Eqn 4, may be related to the more common definition of contrast in terms of the difference in optical densities on two positions on the film. The effective exposures (Eqn 2) can be related back to film densities via the modified characteristic curve (Fig. 2) to predict the contrast given by the difference in optical densities. Object contrast given by Eqn 4 differs from radiation contrast (*i.e.* contrast defined in terms of difference in intensity within the primary beam) in that the sensitivity function of the image receptor is included.

One problem with the usual definition of contrast is that it is dependent on exposure level. The measured film contrast will decrease if the film is substantially underexposed or overexposed, resulting in densities in the toe or shoulder of the characteristic curve, respectively. This definition of contrast (Eqn 4) is independent of radiation exposure level.

This method can be used to predict object contrasts directly from a knowledge of the X-ray spectrum and the sensitivity function of the film-screen combination. To obtain the input radiation contrast (*i.e.* not taking into account the response of the film-screen combination) $S(E)$ may be constrained to be unity for all values of E.

Contrast detail test object design

A computer program was developed (using the Turbo Pascal version 4.0 language on an IBM PC-AT compatible computer) to model the physical conditions and interactions between the incident X-ray beam, aluminium filter, test object and film-screen combination.

Commercially available foils (Goodfellow Metals, Cambridge) were used in the construction of the test object and aluminium tube filter. Whilst it is possible to roll a foil of any specified thickness, this can be expensive. Thus, the test object was manufactured from foils available in the catalogue. The contrasts of these foils were calculated using the above computer program. In certain circumstances, due to the lack of a suitable single foil, it was necessary to use a combination of foils of different materials so that the desired small difference in contrast between neighbouring discs could be achieved. The contrast detail phantom has been designed for use with a 3 mm aluminium filter placed at the tube head. A filter is used in combination with the test object. Therefore, for a given optical density on the film, the X-ray exposure technique factors required for imaging the phantom are comparable with those used in clinical practice for a typical breast. The filter is placed at the tube head so that the effect of scattered radiation on film contrasts is minimized.

The mammographic test object contains a series of discs of varying contrasts and diameters (Table I). The choice of diameters is intended to reflect features of significance in a mammogram, such as low contrast tissue masses of the order of a centimetre in size and higher contrast small objects such as calcifications.

Table I. Predicted radiation contrasts for a 28 kVp contrast potential waveform with 0.03 mm molybdenum and 1.0 mm beryllium filtration

	Radiation contrast	
	Range of disc sizes (mm)	
Disc number	9–3	2–0.5
1	0.0180	0.2186
2	0.0142	0.1866
3	0.0122	0.1395
4	0.0108	0.1179
5	0.0100	0.0956
6	0.0088	0.0746
7	0.0079	0.0463
8	0.0071	0.0396
9	0.0059	0.0283
10	0.0049	0.0243
11	0.0039	0.0180
12	0.0031	0.01225
13	0.00234	0.00883
14	0.00195	—

Although it is desirable to image calcifications as low as 0.1 mm, manufacture of such small objects was not practicable. For larger diameter discs, theory and practice indicate that the threshold contrast varies slowly with increasing diameter and may even tend towards a constant value (Chesters, 1982), so that adding extra larger discs would not supply any extra information.

The input radiation contrast to the film-screen system due to each disc is calculated using the contrast prediction program, so that a table of disc number versus contrast can be created. If desired, the contrasts can be calculated for spectra varying in steps of 0.1 kV. The film reader may refer to the appropriate table to obtain the contrast of the last visible disc. According to the theoretical model, an error of 0.2 kV in measuring the tube potential will introduce an error of only 1% in the contrast predicted.

The disc thicknesses for the large diameter objects have been chosen so that the contrast differs by about 10% from one disc to the next. Manufacturing difficulties dictated the thicknesses of the smaller discs making contrast steps about 23% on average.

Another advantage over commercially available contrast detail tests objects is that the use of a particular tube potential is not critical to obtaining the relevant data. For example, if the nominal and actual tube potentials on a particular X-ray set do not coincide, and it is not possible to expose the test object to a beam of X-rays generated at 28 kVp, the contrast prediction program allows for the disc contrasts to be calculated at other values of tube potential and generator waveform. It is anticipated that the user would be supplied with a set of tables giving the contrast of each disc for a range of tube potentials and generator waveforms.

It was decided to include features in the test object other than the discs used for contrast detail measurements. Hence, while the test object has been designed primarily for contrast detail measurements, it is also possible to assess other aspects of performance from the same radiograph. Figure 3 shows the layout of the mammographic test object. The basic features of the test object are as follows; a lead strip, to allow for a sensitometric exposure for film processor monitoring, a series of discs of varying attenuation and diameter, to be used for contrast detail work, two orthogonal low contrast edges, for measurement of modulation transfer function

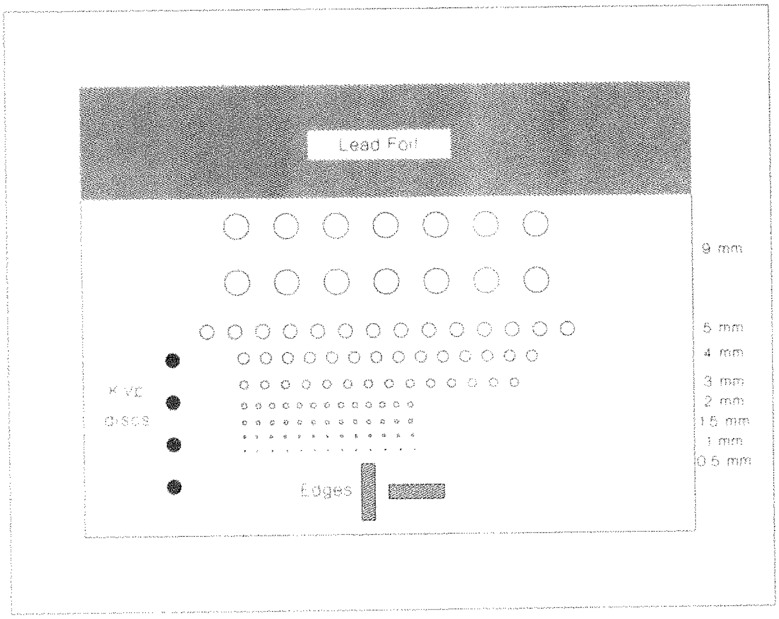


Figure 3. Mammographic contrast detail phantom.

parallel and perpendicular to the anode-cathode axis, a series of discs, to provide known attenuation steps and a uniform region for image noise assessment. The various objects and foils are sandwiched between two 3 mm thick Perspex sheets, which offer rigid protection and introduce a minimum of scattered radiation onto the film. The rectangular shape of the test object allows for easy positioning on top of the image receptor to be assessed. The test object and image receptor are placed on the cassette table on the mammography unit and hence above the grid. The image receptor may be a film-screen combination in a cassette, a film in a light, tight evacuated plastic envelope, or even a xeroradiographic cassette.

Materials and methods

Verification of the contrast prediction model

The sensitivity function for a particular film-screen combination was estimated rather than measured. Conversion of incident X-ray photons to film density is a complex process involving: (1) absorption of energy in the screen phosphor; (2) the efficiency of the conversion of absorbed energy to light; (3) interaction of light with the film.

The absorption of energy in the screen, the first of the above, can be calculated according to the theory described by Birch et al (1979). The latter two stages of the conversion of X-ray photon to film density have been described by Vyborny et al (1980b). Combining the absorption spectrum with the relative efficiency allows the estimation of the relative exposure to give a density of 1.0 optical density units and, hence, an estimate of the sensitivity function $S(E)$.

This method was tested using previously published data. The energy absorption for a gadolinium oxysulphide (GdO_2S) fluorescent screen (Kodak Lanex Regular) is given by Birch et al (1979). This is combined with the relative efficiency data (Vyborny et al, 1980b) to give the estimated sensitivity function. The sensitivity function for a mammographic system, namely an Agfa MR Detail screen and Kodak SO 177 film, was generated. As the Agfa MR Detail phosphor is GdO_2S, it is anticipated that the energy dependence of the relative efficiency curve for this system will be similar to that for the Lanex screen and RP/S film. This assumption is consistent with the experimental results of Vyborny et al (1980b), who found that the relative efficiencies of the three phosphors containing GdO_2S was similar within experimental errors. It is also assumed that the density on film is almost entirely caused by light emitted by the screen (Arnold, 1979).

In order to verify experimentally the accuracy of the contrast prediction model, it was decided to measure the film densities and thereby determine image contrasts on an image of a known set of objects. Therefore, it was decided to radiograph the mammographic test object using Agfa MR Detail screens and Kodak SO 177 film. A radiograph was taken on a CGR Senographe 500T mammography X-ray unit, operating at a measured tube potential of 28.2 kVp, with 3 mm of aluminium filtration placed at the tube head to minimize scatter. The mammographic test object was placed on top of a cassette containing the Agfa MR Detail screens and Kodak SO 177 film. The test object and cassette were placed on top of the cassette holder on the X-ray unit (*i.e.* above the usual position of the cassette and grid). Film density measurements were performed on a Parry densitometer.

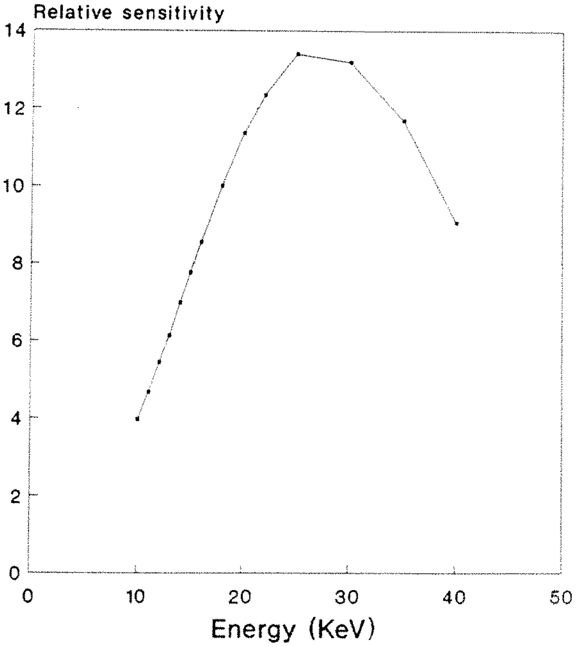


Figure 4. Estimated sensitivity function for Agfa MR-Detail and Kodak SO 177 screen-film combination.

The screen absorption can be estimated using a knowledge of the thickness of the phosphor in the MR Detail screen (Van Esch, 1988). The resulting estimate of the sensitivity function for the MR-Detail-SO 177 system is shown in Figure 4.

Contrast detail performance measurements

The contrast detail performance of a Fuji Hi Mammo screen in a Fuji MA cassette, used with Fuji MINH and Fuji MIMA films, was investigated. In addition, the performance of Kodak SO 177 film in an Agfa Mammoray cassette/MR Detail screen and Fuji MA cassette/Hi Mammo screen was also studied. Exposures were performed on a CGR Senographe 600T mammography X-ray unit. The test object was positioned on top of the film screen cassette with lead foil to the rear, both being placed on the upper surface of the cassette holder. The attenuator foil was attached to the tube housing at the position of the beam collimation aperture to minimize the effect of scattered radiation on the film. Manual radiographic exposures were performed which resulted in an optical density of approximately 1.4 at a position on the film just to the left of the two edges. A

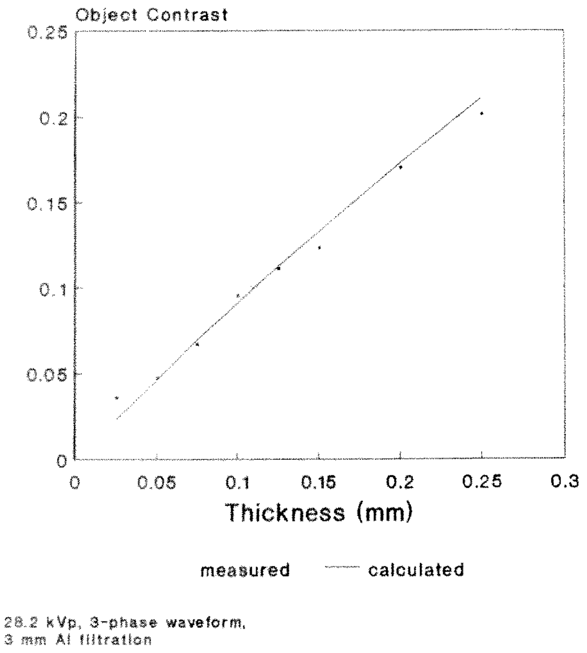


Figure 5. Comparison of predicted and measured fractional contrasts of objects radiographed using the Agfa MR-Detail/Kodak SO 177 screen-film combination.

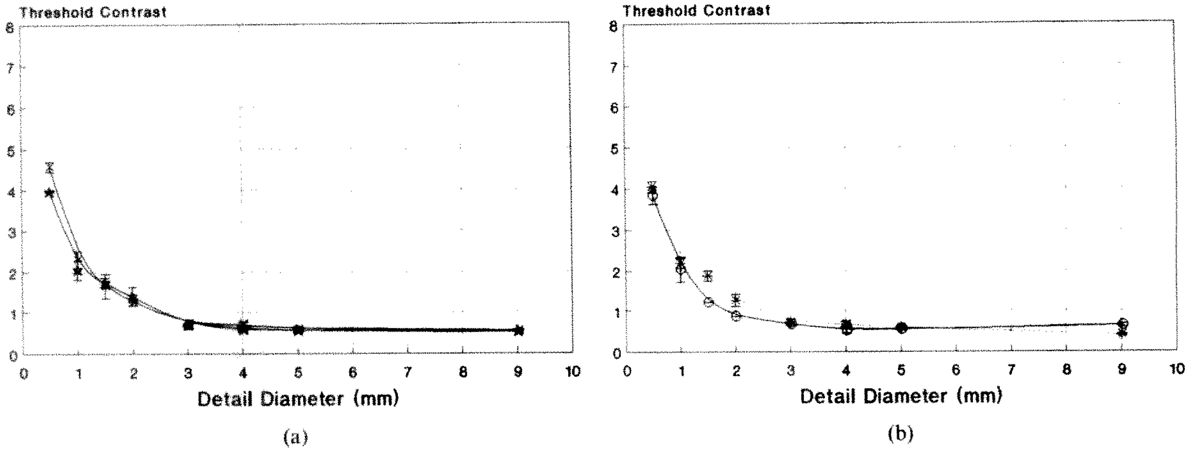
nominal tube potential of 28 kVp was selected. An RMI 232 digital mammographic kVp meter was used to measure tube potential. The kVp meter had been calibrated using the method of Law et al (1989). The measured tube potential was 28.8 kVp. Film processing was performed on a Dupont Cronex T5A processor using a 2.5 min developing cycle, with a developer temperature of 35°C and Kodak chemistry.

The films were read once on 5 different days by a single reader. The ambient light level in the room was approximately 55 lux and the viewing box brightness was 1750 cd m^{-2} (both measured using a Hagner photometer). The film reader viewed each row of discs of a particular diameter to determine the point at which a disc is no longer visible above background noise. The contrast of the last disc detectable represents the threshold contrast detectability of circular objects of that diameter. If the reader is unsure as to the presence of a particular disc a half score may be used. The threshold contrast is interpolated from the table of contrast appropriate to the measured tube potential and generator waveform.

Results and discussion

The measured and calculated contrasts of details within the mammography test object, when imaged using an Agfa MR Detail/Kodak SO 177 screen-film combination, were compared and the results are summarized in Figure 5. Figure 5 shows that there is good agreement between the measured and estimated contrast values with the exception of the smallest disc. The mean percentage difference between the measured and predicted contrast values is under 4%. Therefore, it is concluded that the contrast prediction programme is accurate within anticipated experimental uncertainties. Furthermore, the assumption made in the theoretical contrast prediction program, that scattered radiation has little effect on the film contrasts when using the mammographic test object with the attenuator placed at the tube housing, has been verified experimentally.

Measured contrast detail curves for the four film-screen cassette combinations are summarized in figures 6a and b. From Figure 6a it can be seen that the contrast detail performance of the Fuji MIMA film is slightly better than the Fuji MINH film, when used in



(a)

(b)

Figure 6. (a) Contrast detail performance of two film screen combinations. (× Fuji MA cassette/Hi-Mammo screen and Fuji MINH film, ☆ Fuji MA cassette/Hi-Mammo screen and Fuji MIMA film). (b) Contrast detail performance of two film screen combinations. (* Agfa Mammoray cassette/MR Detail screen and Kodak SO 177 film, ○ Fuji MA cassette/Hi-Mammo screen and Kodak S0 177 film).

conjunction with Fuji Hi Mammo screens and Fuji MA cassette. For objects smaller than 5 mm, the performance of the Kodak SO 177 film in the Fuji screen/cassette was better than with the Agfa screen/cassette. However, for 9 mm circular details the minimum detectable contrast is lower for the Kodak SO 177 film and the Agfa screen/cassette, representing better imaging performance. The shape of the contrast-detail curves (Figs 6a & b) are similar to those observed on other radiological imaging systems, for example image intensifiers (Hay et al, 1985). However, as might be anticipated, the contrast detail performance of the mammographic film-screen combinations investigated here represent improved performance, when compared with an image intensifier television system.

An important aspect of the design of this test object is that the object contrasts are estimated accurately, given a knowledge of the tube potential and generator waveform. These object contrasts have been verified experimentally within anticipated errors. Comparative contrast detail measurements can be made on any mammography units and image receptors.

In the main, the percentage difference in contrast between adjacent discs of the same diameter and the percentage difference in size between adjacent rows of discs, are less than on other contrast detail test objects (Hay et al, 1985, Cowen et al, 1987). It is considered that this design feature will enable the test object to discriminate small differences in contrast detail performance, which will be particularly useful in mammography.

The test object has been designed for use with an attenuator placed at the tube housing, an experimental arrangement which minimizes the effect of scattered radiation on the image. The test object could be used in conjunction with scattering media, such as Perspex, but significant amounts of scattered radiation will affect object contrasts which will no longer be known accurately. The test object could, of course, still be useful in image quality assessment in the presence of scatter, as the total number of discs or image score could provide interesting information. However, the quantitative values of object contrast are lost, making the results harder to interpret. Changes in image score could arise from alterations in imaging performance or be an artefact due to scatter.

Summary and conclusions

A test phantom has been designed for use in image quality assessment of mammographic imaging systems. Discs of various sizes and contrasts have been incorporated in the test object. This test object is intended for the measurement of contrast detail performance in mammography, in which the effect of scattered radiation on the image receptor has been minimized. In these circumstances, and provided the tube potential and generator waveform have been measured accurately, the object contrasts of the various discs are also known accurately. The test object is not limited to use at one combination of tube potential and generator waveform. Separate calculations and experimental measurements have been performed to verify the accuracy of the contrast prediction model. The test object may be used in the presence of scattered radiation, but this will affect the quantitative values of object contrast.

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Technical note

Three-dimensional (3D) ultrasound imaging of the gallbladder and dilated biliary tree: reconstruction from real-time B-scans

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Ultrasound is perhaps the most operator-dependent imaging technique. Clinicians rarely master the interpretation of ultrasound images and even experienced ultrasonographers may experience difficulty interpreting "hard copy" images produced by other operators. Reconstructed three-dimensional (3D) computer images of computed tomography (CT) scans have been shown to aid interpretation of CT data by clinicians, particularly before reconstructive and orthopaedic surgery (Lafferty et al, 1986; Linney et al, 1989). We propose that similar reconstruction of ultrasound images may aid clinicians' understanding of the anatomy of the enlarged biliary tree and gallbladder.

Method

Ultrasound studies of the biliary tree were performed using a Toshiba 100 real-time ultrasound system with a 3.5 MHz curved array transducer. The probe was located on the skin surface, then smoothly rotated by hand at the probe face so as to obtain a continuous, sequential sweep across the volume of the liver. The sequence of B-scans obtained was recorded on videotape. The angle of rotation of the probe was estimated by eye. Regular sample frames of the videotaped data were selected for digitization by frame by frame examination of the videotaped data. Images were digitized using an Oggitronics 8-bit recursive video processor. The images were transferred to a DEC VAX 11-730 minicomputer and SIGMEX A7000 display processor, running the Southampton General Hospital PICS general image processing software (Fleming et al, 1987). Images were compressed to 256 × 256 pixel square matrix format. In each study, 20–30 sample images were taken.

Location of the B-scan pixels in true 3D space, allowing for the rotational sweep of the probe, was achieved by defining the location of each B-scan in a cubic matrix with sides of length equivalent to 256 pixels. The axis of rotation (defined as the probe surface) was located at or near the edge of this cubic matrix. The individual slice images were placed in the 3D matrix and rotated in 3D space with respect to the neighbouring slices. The angle of rotation between each slice was calculated from the total rotation of the probe and the number of sample slices selected. Empty 3D elements or voxels were defined by interpolation from adjacent filled voxels. Finally, a new set of parallel slice B-scan images were defined from the data in the 3D matrix.

Individual B-scan images were smoothed by median filtering where pixel values were replaced by the median value of pixel intensities in the 7 × 7 square matrix centred on that pixel. Images were thus smoothed while preserving the sharpness of boundaries between bile duct and parenchyma. A corresponding map of the variation of gradient over the B-scan image was created using the sobel gradient filter. The contrast of bile ducts against the surrounding parenchyma was improved by weighting the pixel intensity according to the proximity to, and the amplitude of, nearby gradient maxima. Bile ducts were then identified by simple thresholding, with manual assistance where necessary. A 3D voxel based database of bile duct geometry was created from the B-scan images, with interpolation of the occupied volume between B-scan slices. 3D projection and surface rendering with hidden surface removal was performed using a Z-buffer technique (Gordon & Reynolds, 1985). Perpendicular projections from the image plane were taken into the 3D matrix to locate the nearest object surface and create a matrix of surface depths. This was then used to provide surface shading by a combination of inverse distance and angle shading, using Lamberts law for non-specular reflection. Series of 3D projected images at different viewing angles were displayed at video rates so as to provide a realistic impression of object rotation.

Results

Figure 1 shows a 3D reconstruction of a gallbladder at four separate viewing directions, with a 30° rotation between views. The front structure of the gallbladder was rendered translucent so as to reveal the presence of the calculi. The apparent flatness of the gallstones is

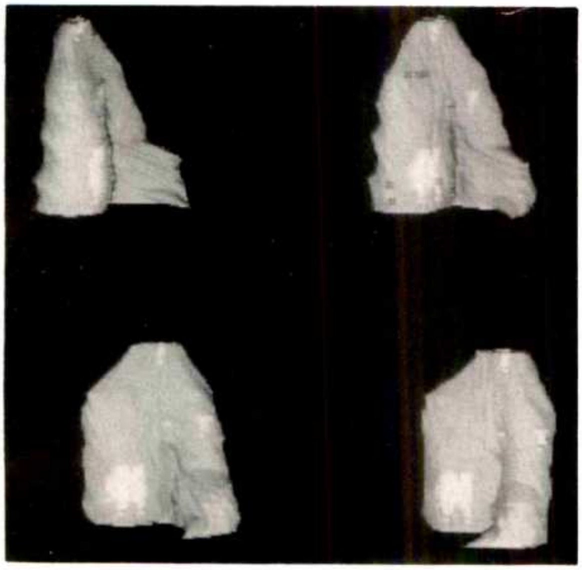

Figure 1. Four 3D reconstructed views from an ultrasound study of a gallbladder containing calculi. A rotation of 30° was applied between views.

probably artefactual, resulting from the dominance of the specular reflection in the original ultrasound images.

Figure 2 shows a similar reconstruction of a dilated biliary tree. The common hepatic duct, right and left intrahepatic ducts and their main branches are shown, as is the gallbladder. Figure 3 shows a reconstruction of a cadaver biliary system imaged by CT and ultrasound. For CT, the biliary system was revealed by injection of contrast agent into the common hepatic duct. The CT 3D projection shows more detail, but the basic anatomy presented by both imaging modes conform.

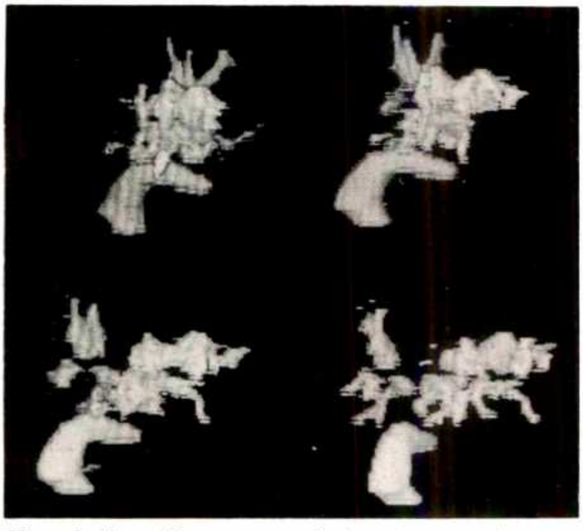

Figure 2. Four 3D reconstructed views from an ultrasound study of a dilated biliary tree. A rotation of 30° was applied between views.

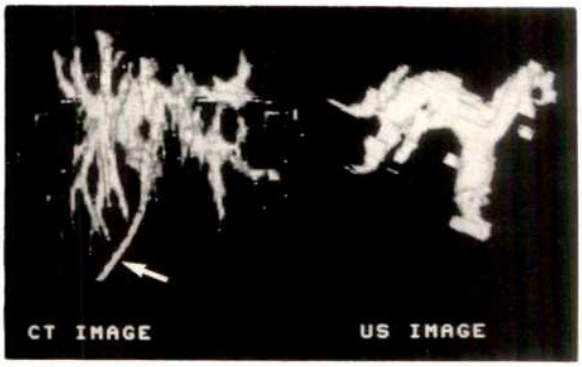

Figure 3. A comparison of 3D views of a cadaver liver reconstructed from CT and ultrasound source data. The catheter through which contrast was added for CT imaging is marked.

Discussion

3D reconstructions of real-time ultrasound B-scans of the biliary tree and gallbladder have been produced using a general purpose computer system and image processing software. The images produced thus far are not of diagnostic quality. Improvement could be achieved by direct input of digital signals from the ultrasound machine. The main handicap to reliable representation of 3D geometry is the lack of true image registration data in real-time ultrasound B-scan imaging with an unrestricted, hand held probe. The use of a mechanical arm system to monitor the location and orientation of the probe during image acquisition would facilitate the alignment of B-scan images. This would allow the reliable location of anatomy revealed in B-scan images in 3D space.

Further developments of this technique may facilitate teaching and allow ultrasonographers to communicate their findings in a form easily accessible to clinicians.

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Case reports

Neonatal hepatic calcification in subcapsular haematoma with hydrops fetalis

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Keywords: Neonatal, Hepatic, Calcification

There are many causes of fetal and infant hepatic calcification. We present two cases of hepatic calcification in a subcapsular haematoma in neonates with hydrops fetalis and chromosomal abnormalities. We do not believe that such an association has been described previously.

Case reports

Case 1

A 22-year-old woman presented at 30 weeks gestation with polyhydramnios. An ultrasound scan at 14 weeks had shown no abnormality. A scan at 30 weeks showed gross fetal ascites and a diagnosis of non-Rhesus hydrops was made. The pregnancy was allowed to continue and a normal vaginal delivery occurred at 33 weeks. A female infant with external features of Down's syndrome was delivered. Chest and abdominal radiographs taken on the first day showed areas of reticular calcification in the right upper quadrant (Fig. 1). An ultrasound examination on the fourth day showed this calcification to lie on the liver surface and to be concentrated mainly around the porta hepatis. There was gross ascites but no other areas of calcification could be seen (Fig. 2). An ultrasound scan of the brain was normal. There was no growth of organisms from blood or ascitic fluid and antibody titres for varicella and toxoplasmosis, rubella, cytomegalovirus and herpes simplex (TORCH) complex viruses were negative. On the fifth day of life she became cyanotic and died. Trisomy 21 was confirmed cytogenetically.

Case 2

A 27-year-old woman presented at 18 weeks gestation for a routine antenatal ultrasound scan. This showed a very oedematous fetus with gross ascites and a probable cystic hygroma. The liver was not noted to be abnormal. The parents elected for termination of the pregnancy and labour was induced with the delivery of a small for dates, female fetus.

Pathology

Case 1

The body was that of a female infant whose external measurements and body weight were consistent with a gestational age of 33 weeks. There was peripheral cyanosis and gross ascites. The thorax and upper limbs were oedematous. The infant had a flat occiput, a mongoloid face and brushfield spots in both eyes.

On internal examination the lungs were firm and congested, and the liver showed some calcification close to the porta hepatis and just below the capsule. There were no congenital abnormalities. On histology the lungs showed marked alveolar collapse, interstitial emphysema and hyaline membrane disease. The liver (Fig. 3) showed subcapsular fibrosis with dystrophic calcification extending to the large portal tracts. The calcification was not related to blood vessels. This appearance was most likely to represent an organizing fibrosed subcapsular haematoma. The liver parenchyma distal to this was normal and there was no evidence of increased hepatic haemopoiesis. Such an increase could, however, have occurred *in utero* and this would not be detectable at post-mortem.

Case 2

The body was that of a female fetus whose external measurements and body weight were consistent with a gestational age of 16 weeks. There was a moderate degree of hydrops fetalis

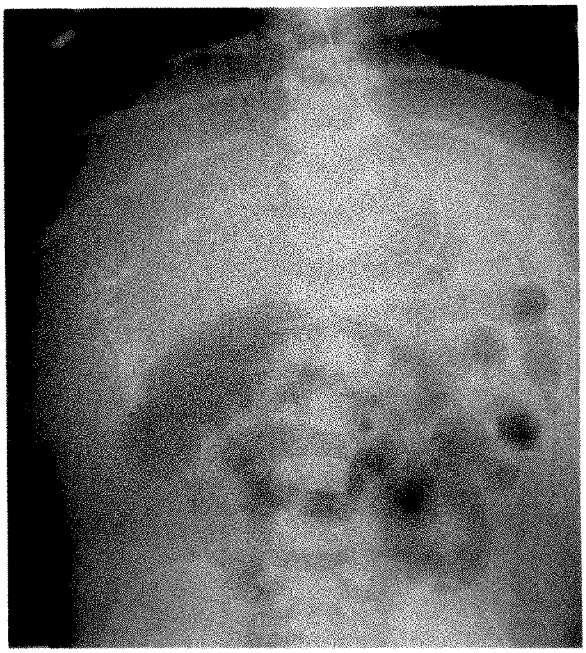

Figure 1. Plain abdominal radiograph showing reticular calcification overlying the liver.

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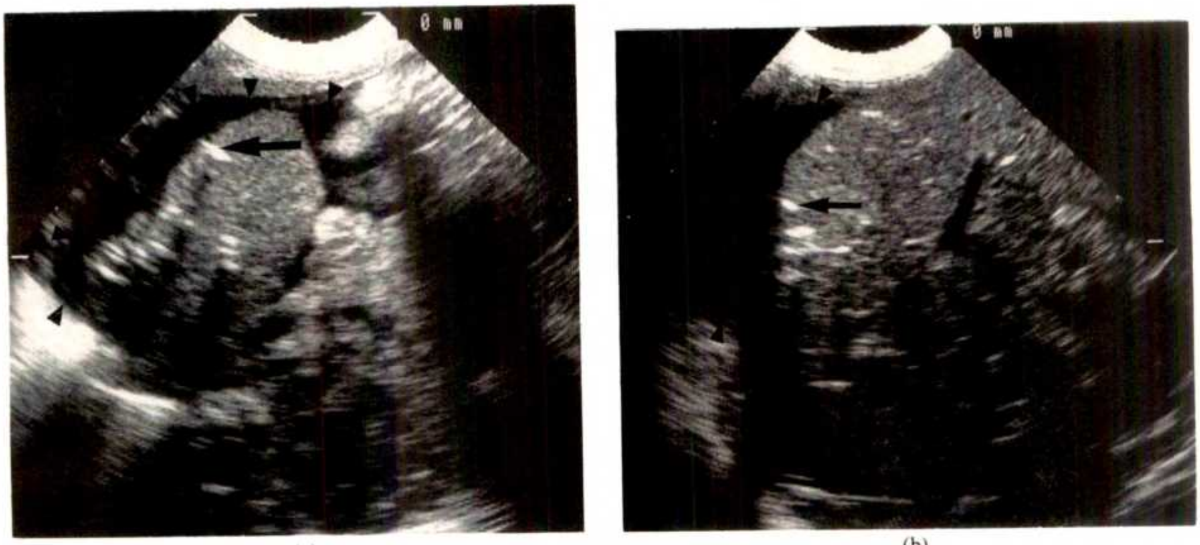

(a)

(b)

Figure 2. (a) Longitudinal and (b) transverse ultrasound scan sections through the liver showing areas of calcification (arrow) and ascites (arrowhead).

and a large cystic hygroma. There were no dysmorphic features but the fetus was shown to have Turner's syndrome (monosomy XO) on cytogenetic testing.

On internal examination the only congenital abnormality was a single horseshoe kidney. A small focus of calcification was noted along the lower border of the liver, which was shown microscopically to be a partially organized and calcified subcapsular haematoma.

Discussion

Both of these cases show subcapsular calcification related to a haematoma which, as far as we are aware, has not been described previously as a cause of neonatal hepatic calcification. There are many causes of hepatic calcification which have been described in this age group.

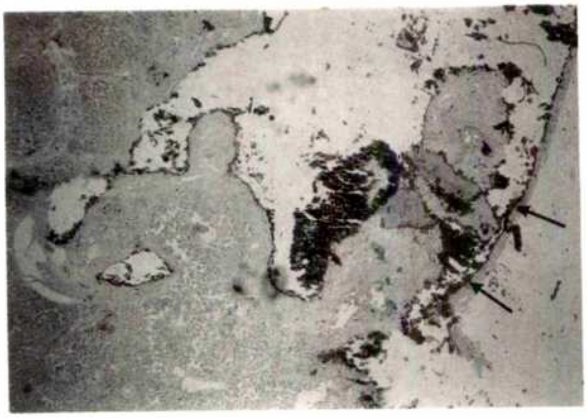

Figure 3. Histological section of liver of Case 1 showing subcapsular calcification (arrowed) [haematoxylin and eosin stain, × 101].

Calcified portal vein thrombi (Blanc et al, 1967; Friedman et al, 1981) tend to produce branching peripheral calcification and are often associated with other congenital abnormalities. In our first case the plain radiograph showed central reticular calcification and histology confirmed that the calcification was not related to vessels.

Ischaemic infarcts (Nguyen & Leonard, 1986) and thrombi following umbilical vein catheterization (Ablow & Effman, 1972) are distributed throughout the liver and show no pre-dilection for a peripheral or lobar distribution. The calcification is usually distributed throughout the liver parenchyma.

Meconium peritonitis (Forouhar, 1982; Lince et al, 1985) is a common cause of abdominal calcification. This is usually scattered throughout the abdomen, although it may be confined to the liver surface. There was no evidence of ileus or peritonitis in our cases.

Transplacental infection with TORCH complex viruses can cause a neonatal hepatitis which may show scattered nodular hepatic calcification and usually affects several organs (Shackleford & Kirks, 1977). There was no evidence of infection in our case.

Tumours of the liver show a complex mass on ultrasonography which may or may not have areas of calcification within it (Moss et al, 1971; Cremin & Nuss, 1974). This was not present in our cases. Birth trauma is known to cause subcapsular hepatic haematoma but in both our cases this was not a factor and in Case 1 insufficient time elapsed between birth and death for calcification to occur.

Conclusion

Hepatic calcification in the fetus or neonate is evidence of serious disease that can be detected on radiological or ultrasonographic examination. The distribution and appearance of this calcification, and its presence or absence at other sites, may enable a diagnosis to be made.

The two cases presented do not fit into previously described categories. We propose an additional cause of neonatal calcification; that is dystrophic calcification arising in a subcapsular haematoma. Both of our cases presented with hydrops fetalis and had a chromosomal abnormality. The significance of these findings in the pathogenesis of hepatic calcification is uncertain. We would, however, suggest that the anaemia found in hydrops fetalis stimulates hepatic haemopoiesis and this, in turn, renders the liver more susceptible to subcapsular haematoma formation which subsequently calcifies. Neonatal hepatic calcification and hydrops fetalis may, therefore, be a new association.

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Oesophageal ruptures complicating balloon dilatation of strictures: a report of two cases

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Keywords: Oesophageal perforation, Balloon dilatation

Balloon dilatation of upper gastro-intestinal tract strictures is accepted as a safe and effective method of dealing with lesions of varying aetiology. Perforation of the oesophagus is a recognized, but rare complication. Two such cases are described and their management is discussed.

Case 1

A 67-year-old man with a 10 year history of hiatus hernia associated with an oesophageal stricture presented with dysphagia and coughing after swallowing. Endoscopy revealed a benign oesophageal stricture at 35 cm.

Dilatation was performed using a 22 mm Lunderquist-Owman oesophageal dilatation kit (William Cook Europe) balloon under intravenous sedation (6 mg Midazolam Hydrochloride). The balloon was distended three times with ease under fluoroscopic control and no waisting of the balloon was visible on the final dilatation.

The patient complained of pain 4 h after the procedure and a chest radiograph was taken revealing no abnormality. The following morning a further chest radiograph revealed extensive consolidation in the left lower lobe.

A water soluble contrast swallow demonstrated a leak from the lower oesophagus. The patient was treated by bed rest and intravenous fluids for 1 week and no surgical intervention was required. The patient was discharged well on the seventh day following the procedure.

Case 2

A 59-year-old lady presented with lower oesophageal dysphagia. At endoscopy there was an impassable area of narrowing in the lower oesophagus. Biopsies revealed no evidence of malignancy.

After clinical discussion it was decided to perform a balloon dilatation of the stricture to alleviate the symptoms. Endoscopy of the whole lesion was planned for a later date.

The dilatation was performed under intravenous sedation (6 mg Midazolam Hydrochloride). A balloon catheter was passed easily beyond the lesion under fluoroscopic control. No guide wire was used to negotiate the stricture.

A balloon catheter (Lunderquist-Owman oesophageal dilatation kit, William Cook Limited) was inflated twice to its maximum diameter of 22 mm. On the first inflation there was some waisting in the balloon outline but this was not seen at the second inflation.

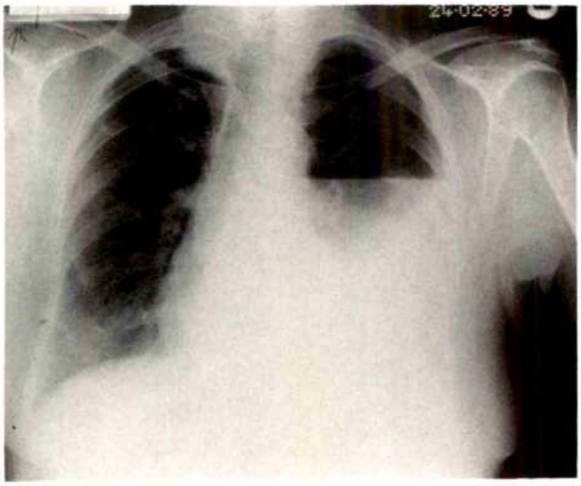

Figure 1. Postero-anterior chest radiograph showing a left-sided hydropneumothorax.

The patient complained of some upper abdominal discomfort and shortness of breath 4 h after the procedure. A chest radiograph was taken with poor inspiration but this revealed no abnormality.

After overnight observation, examination revealed some epigastric tenderness but no guarding. The patient was dyspnoeic at rest. A second chest radiograph was taken 23 h after the procedure (Fig. 1) and this revealed a large, left-sided hydropneumothorax. At operation a 4 cm × 2 cm defect was found in the oesophagus and repaired. A water soluble contrast study performed 3 days after surgical repair showed no evidence of a leak and free flow into the stomach. The patient was finally discharged 2 weeks later.

Discussion

Rupture of the oesphagus during balloon dilatation is uncommon. The radially directed forces generated are thought to be safer than the longitudinal forces produced during bouginage. Some authors have concluded that the risk of rupture is "virtually eliminated" by this technique (Starck et al, 1984). There is a report of perforation by guide wire (Dawson et al, 1984). Both Gotberg (1982) and La Berge (1985) reported a single case of rupture during balloon dilatation. Maynar et al (1988) reported three ruptures in 170 procedures (2%) involving 35 patients. McLean and LeVeen (1989) demonstrated the reduced shearing forces of balloon compared with bougies *in vivo* and concluded that balloon dilatation would be expected to have a higher margin of safety. We have experienced two ruptures in a series of 46 procedures in 33 patients. The rupture may not be apparent immediately after the procedure, and in the case reported by La Berge et al (1985) the patient had been discharged home. In our cases the balloons were inflated with ease and the patients did not suffer undue discomfort. Most patients experience chest tightness during inflation but the use of intravenous sedatives and/or analgesics makes it very difficult to quantify this.

Evidence of bleeding is commonly seen on the balloon after removal. Grundy and Belli (1988) recommended that a chest radiograph be performed 2–3 h after the procedure and, if normal, that the patient be allowed to eat and drink. La Berge et al (1985) observed their patients for only 1 h. The disturbing feature of our cases was that chest radiographs taken 3–4 h after the procedure showed no abnormality, while those taken after 20 h revealed obvious abnormalities. While it is impractical to keep patients fasting for 24 h routinely, we now only perform this procedure in the morning and post dilatation chest radiographs are taken no less than 6 h after the procedure. If there is any evidence of pleuritic or abdominal symptoms, overnight observation in hospital is advocated, and if symptoms persist we repeat the chest radiograph next morning. If doubt persists a water soluble contrast study can be performed before allowing any fluid or food by mouth.

The risk of perforation is probably higher than generally realized and this may be increased when the newly introduced larger balloons of up to 3 cm in diameter are more widely used (William Cook Limited). The post procedural clinical observation of the patient is vital. The chest radiograph is essential but it must only play a part in the patient assessment process. There is pressure to perform this procedure as a day case and this can often be done. The patient's discharge should be supervised by an experienced clinician and facilities to observe the patient overnight should be available if required.

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Paget's disease of the male breast treated by radiotherapy

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Keywords: Paget's disease, Male breast, Radiotherapy

Breast cancer is a rare disease in men; the female : male ratio is around 100 : 1 (Treves, 1954; Haagensen, 1986). Aetiological factors in male breast cancer are obscure. A marked increase in its incidence has been reported in Klinefelter's syndrome, a condition associated with diminished testosterone levels and an increased incidence of gynecomastia (Rosen et al, 1976; Erlichman et al, 1984).

Paget's disease of the nipple is an early presentation of breast cancer (Nance et al, 1970). In this report, we describe a case in a 74-year-old patient. Since carcinoma of the male breast is a relatively rare malignancy, it is reasonable that the management of this disease should be based on the knowledge available for carcinoma of the female breast. Breast conserving treatment in females has been demonstrated to be equivalent to radical surgery. Therefore, we suggest that radiation therapy is the treatment of choice also in male patients with Paget's disease, as was done in the case reported.

Case report

A 74-year-old man noticed, for 1.5 years, an itching painless lesion under the left nipple. There was no family history of breast cancer. On physical examination an erythematous, slightly desquamating area measuring 5 × 2.5 cm was found. There was no palpable mass or lump in the breast. There was no discharge or bleeding. The right breast was normal. There were no palpable lymph nodes in the axillae. The general observation showed no metastases. On 31/10/1988 a biopsy was performed for diagnosis. The histological examination showed the presence of several, large atypical cells, both single and in small clusters, distributed throughout the epidermis. These cells were characterized by their irregular nucleus and large clear cytoplasm. On immunostaining these cells were strongly positive with antisera directed against human milk fat globulin. In the Paget's cells S100 protein was not detectable. The patient was treated with radiation therapy from 06/12/1988 till 23/01/1989. He received a dose of 66 Gy to the chest wall (initial field size of 125 × 135 mm, boost of 99 × 107 mm) with electrons. The regional lymph nodes were not treated.

During the treatment regression was seen and at first follow-up the tumour had disappeared. The initial lesion has remained in regression and in May 1990 only a depigmented area was visible.

Discussion

Paget's disease of the breast is a scaling or eczematoid lesion of the nipple and the areola, sharply limited, caused by invasion of the epidermis by a malignant tumour of the caniculi of the breast. The most frequent presenting signs are ulceration and eczematous change of the nipple; other findings are discharge, bleeding and crust formation (Treves, 1954; Ashikari et al, 1970; Nance et al, 1970; Nehme, 1976; Bulens et al, 1990). Two different entities are distinguished: the pure Paget's disease of the breast and a clinical tumour mass associated with the Paget's phenomenon (Rissanen & Holsti, 1969; Kisten & Haagensen, 1970; Nance et al, 1970). The first group contains only changes of the nipple. The second clinical presentation comprises nipple changes accompanied by a palpable breast mass or lump. The tumour is always an underlying invasive tumour (Crichlow & Czernobilsky, 1969; Ashikari et al, 1970). Peak incidence of Paget's disease of the male breast is between 50 and 75 years of age (Maier et al, 1969; Serour et al, 1988). The most common location for the tumour is the nipple, but other locations, such as the surrounding skin, are possible.

The incidence of nodal involvement in patients with Paget's disease limited to the nipple is very low. In the series reported in the literature very few patients with Paget's disease of the breast without an underlying breast tumour have axillary metastases (Paone & Baker, 1981; Fourquet et al, 1987). Pure Paget's disease has an excellent prognosis. The overall survival rate of pure Paget's disease at 5 years varies between 83 and 94.1% and at 10 years between 75 and 87% (Rissanen & Holsti, 1969; Ashikari et al, 1970; Nance et al, 1970; Salvadori et al, 1976). In a patient with a tumour mass, the prognosis is determined by the underlying invasive process.

The definitive diagnosis of Paget's disease is based on the presence of the characteristic Paget's cells in the epidermis. They correspond to large pleiomorphic, atypical epithelial cells with hyperchromatic nuclei and pale cytoplasm. (Maier et al, 1969; Lagios et al, 1984; Serour et al, 1988). The dermis shows reactive changes

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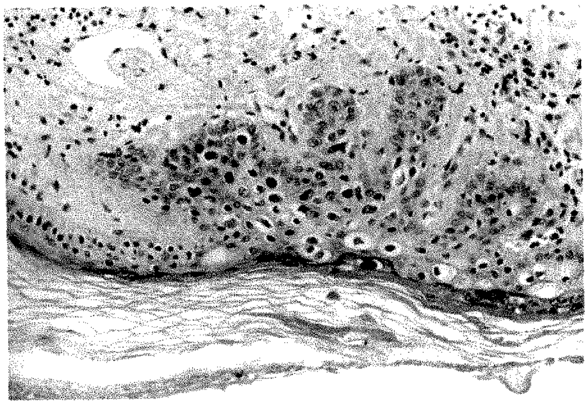

Figure 1. Histological section shows the presence of multiple solitary large Paget's cells dispersed in the epidermis (original magnification × 310).

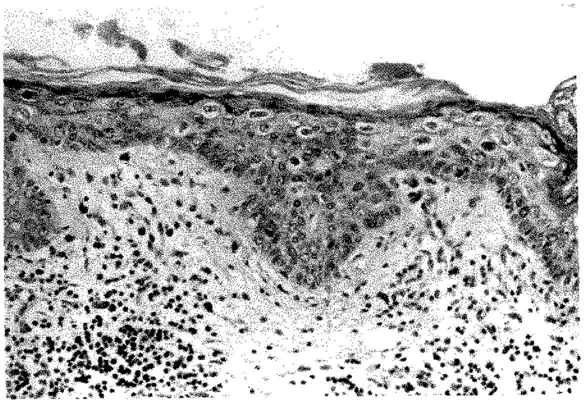

Figure 2. The biopsy illustrates an inflammatory reaction: many lymphocytes around the vascular plexus (original magnification × 310).

only: congestion of the superficial dermal plexus and a perivascular inflammation, which are responsible for part of the clinical picture (Nadji et al, 1982). Electron microscopy demonstrates hemidesmosomal attachments between Paget cells and keratinocytes, supporting the evidence of an intraepidermal origin of Paget cells (Paone & Baker, 1981; Lancer & Moschella, 1982; Fourquet et al, 1987).

In the literature 28 published cases of Paget's disease of the male breast were found (Crichlow & Czernobilsky, 1969; Lancer & Moschella, 1982; Lagios et al, 1984). In 11 patients Paget's disease was associated with a lump. There were only 17 patients with the pure Paget's disease. In the cases reported the treatment was radical or modified radical mastectomy. Post-operative radiotherapy was performed in three of the 17 cases. According to the recent literature we treated this patient with radiotherapy. This is analogous to what is done in female Paget's disease.

Recent data demonstrate that conservative management with radiation therapy is the treatment of choice in Paget's disease of the nipple without detectable breast tumour in the female. In a series of 20 patients with Paget's disease treated with radiotherapy at the Institut Curie, Paris (17 patients were treated with radiation therapy alone after an incisional biopsy for diagnosis) there were only three local recurrences (15%). One patient was salvaged with a modified radical mastectomy and two patients were salvaged with a simple mastectomy. No patient died of breast cancer (Fourquet et al, 1987).

At our institute, 13 female patients with histologically proven Paget's disease were treated conservatively with radiotherapy (without excision of the nipple) between 1971 and 1984 (Bulens et al, 1990). No recurrences locally or at distance were seen until now.

In the European Organization for Research and Treatment of Cancer (EORTC) Breast Group a survey study is presently underway, in which those patients treated without mastectomy are registered and followed. Present data indicate that Paget's disease of the breast can be treated with radiotherapy. This patient is the eighteenth reported in the literature and the only one treated with radiation therapy alone, which is probably the treatment of choice in this rare disease.

In summary, recent findings suggest that mastectomy is unnecessary and that radiotherapy alone has a very important role in the treatment of Paget's disease.

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Relapsing polychondritis: report of an unusual case and a review of the literature

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Keywords: Relapsing polychondritis, Computed tomography

Relapsing polychondritis is an uncommon multisystem disorder, characterized by recurrent inflammation of cartilage at multiple sites, which can go unrecognized until classical signs of cartilage destruction occur. Destruction of the cartilage of the external ears and nose is easy to recognize. Central airway involvement is more difficult to recognize, but more important in terms of prognosis. Neurological symptoms and signs are uncommon, have been infrequently reported and may lead to incorrect diagnosis and delay in treatment.

A case of relapsing polychondritis presenting as an acute encephalitis is described. The use of computed tomography (CT) in determining the presence and severity of central airway involvement is discussed.

Case reports

A 58-year-old man was admitted in June 1988 with a 6-week history of ear infection not responding to three courses of antibiotics. During this time he had been unwell with earache, headache, fatigue and lethargy and was sleeping for long periods. He also had fleeting arthralgia and intermittent fever with rigors. Two days before admission he deteriorated and became confused, uncooperative and drowsy.

He was known to have been under the care of an ophthalmologist with left episcleritis, for the previous 8 months. In 1972, mild asthma was treated with inhaled bronchodilators and in 1983 he experienced costochondral chest pain.

On admission he was found to be drowsy, confused and agitated. Bilateral conjunctivitis, swollen eyelids and tender pinnae were noted but the tympanic membranes were normal. Examination of the central nervous system showed no localizing signs, but formal assessment of functions requiring a cooperative patient was not possible.

Investigations showed a peripheral neutrophilia and raised plasma viscosity, erythrocyte sedimentation rate, C-reactive protein and circulating immune complexes. Autoimmune profile showed a low titre of autoantibodies for anti-nuclear factor and smooth muscle. Immunoglobins, VDRL/TPHA, urea and electrolytes, glucose and liver function tests were normal. Serology, blood cultures, eye and throat swabs and mid-stream urine (MSU) showed no evidence of infection. Cerebrospinal fluid (CSF) showed a lymphocytosis with raised protein, normal glucose and negative gram stain and culture.

A diagnosis of lymphocytic meningo/encephalitis, possibly due to herpes simplex was made on the clinical presentation. Empirical treatment with steroids and acyclovir was started whilst awaiting the results of further serology. The eye and ear signs did not appear consistent with the diagnosis, but were presumed to be due to concurrent polychondritis. Chondritis of the pinnae was later confirmed histologically.

A CT scan of the brain excluded the presence of an intracranial abscess. In view of the persistent cerebral symptoms, magnetic resonance imaging (MRI) of the brain was performed and also found to be normal.

Serology results then excluded an infective cause for his cerebral dysfunction and the acyclovir was stopped. A course of high-dose steroids, reducing over several weeks, was started. There was some improvement over the next few weeks and he was discharged from hospital with residual cerebral damage and personality change.

He was well until April 1989 when he suffered a relapse of the inflammation of the pinnae. Steroids were reintroduced with good effect. A second relapse occurred after stopping the steroids, and now the ears folded over due to destruction of the cartilage of the pinnae.

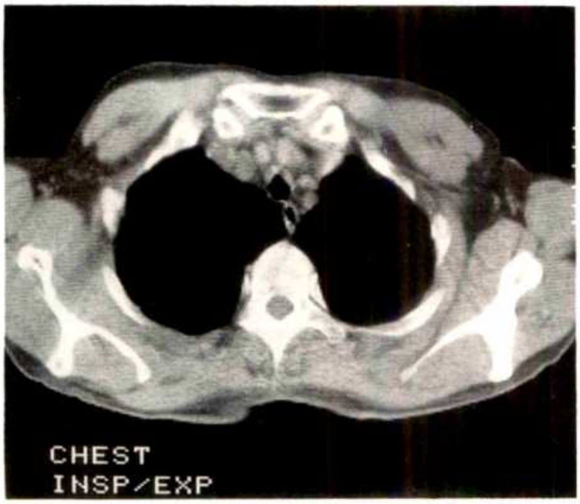

Figure 1. CT scan of the chest (soft-tissue settings). The scan was taken during arrested inspiration and shows irregularity of the wall of the trachea.

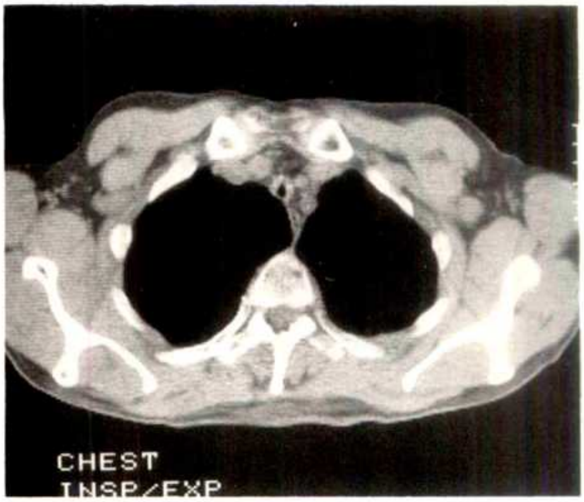

Figure 2. On the expiration CT scan the trachea has collapsed.

In late May 1989, during withdrawal of steroids, he was seen in the outpatient department and noted to have an unproductive cough and some inspiratory and expiratory stridor. Forced expiratory flow rate was reduced (65 litres/min). Tracheal involvement with polychondritis was suspected and he was referred to the chest clinic for an opinion. In early July 1989 a chest radiograph, CT scan of the chest, respiratory function tests and nasendoscopy were arranged.

The appearance of the trachea on the chest radiograph was equivocal. CT of the chest was performed on inspiration by asking the patient to "take a small breath and hold it". Thus inspiration scans were taken with a closed glottis. Expiratory CT was performed by asking the patient to breathe out and the scan was taken after the patient had finished the expiration. CT scan of the chest demonstrated an unusual pentagonal shape to the trachea during held inspiration with thickening of the anterior wall and almost complete collapse during expiration (Figs 1, 2). The major bronchi were also shown to be considerably narrowed on the expiratory phase.

Respiratory function tests, including flow volume studies, confirmed major airway obstruction during both inspiration and expiration, with a normal transfer factor (Table I, Fig. 3). Nasendoscopy demonstrated normal vocal chords and supraglottic structures with a narrowed trachea.

Two weeks later he was admitted after an acute episode of difficult swallowing with choking. The dose of steroids was increased again and azathioprine started. He was referred to the thoracic surgery unit where bronchoscopy showed narrowing of the trachea and major bronchi. A Montgomery t-tube was inserted via tracheostomy to prevent healing of the trachea in a collapsed state. He made a good recovery and was discharged home having been taught management of his airway.

Table I. Respiratory function studies showing severe airflow obstruction but normal transfer factor

		Result	Normal range	After bronchodilator
Peak expiratory flow (litres/min)	PEF	65	382–620	65
1 s forced expired volume (litres)	FEV_1	0.7	2·5–4.2	0.6
Forced vital capacity (litres)	FVC	1.7	3.2–5.2	1.4
Expired vital capacity (litres)	EVC	2.6	—	3.3
	FEV_1%EVC	25	65–88	18
Inspiratory vital capacity (litres)	IVC	3.8	3.5–5.3	—
Functional residual capacity (litres)	FRC	4.2	2.6–4.5	—
Residual volume (litres)	RV	3.6	1.7–3.0	—
Total lung capacity (litres)	TLC	7.4	5.8–8.1	—
CO transfer factor (SI)	T_L,CO,sb	7.9	7.2–11.8	—
Transfer coefficient (SI)	T_L/V_A,eff	1.6	—	—
Maximal expiratory pressure	cmH_2O	+110	> +70	—
Maximal inspiratory pressure	cmH_2O	−78	< −70	—
Flow at 50% FVC (litres/min)	$MEF_{50\%FVC}$	15	138–397	—
Peak inspiratory flow (litres/min)	PIF	132	—	—

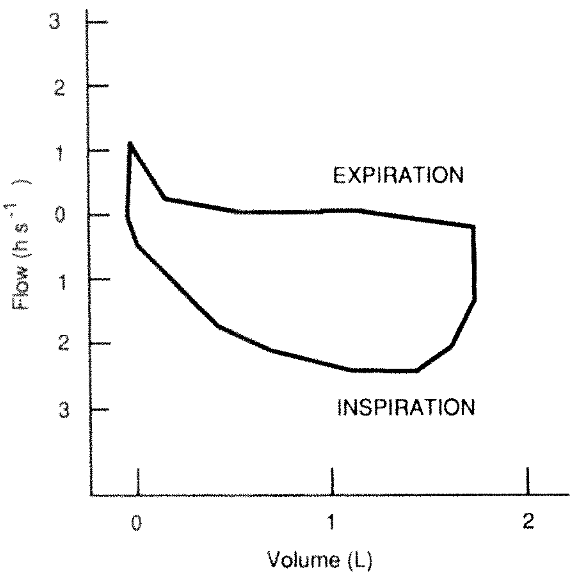

Figure 3. Flow–volume loop showing severe expiratory flow obstruction.

He died suddenly at home on 26 August 1989. Post-mortem examination revealed a correctly sited Montgomery tube occluded by a thick mucus plug extending from the side arm to the carina. The larynx was normal but the trachea was compressible with loss of the normal rigidity provided by the "C"-shaped rings of cartilage. The cause of death was asphyxia resulting from obstruction of the artificial airway by a mucus plug.

Discussion

The case presented is both unusual and informative. The ocular and auricular symptoms and signs, histological findings and clinical relapses are typical of relapsing polychondritis. McAdam et al (1976) presented a series of 23 patients with relapsing polychondritis, reviewed the literature and described the findings as auricular chondritis (88%), arthritis (81%), nasal chondritis (72%), ocular inflammation (65%), respiratory tract inflammation (56%), audio-vestibular damage (46%) and miscellaneous symptoms. Only five of 159 patients reviewed had central nervous system vasculitis. Nasal cartilage involvement occurs at presentation in 13% of patients, but ultimately occurs in 72%. Its absence in this case, despite the severe tracheobronchial involvement, may be unusual.

Presentation with predominantly neurological problems is very uncommon for relapsing polychondritis, but has been described (McAdam et al, 1976). A case of relapsing polychondritis with a neurological presentation and lymphocytic meningitis has been described previously (Stewart et al, 1988), when histological findings suggested a cerebral vasculitis affecting small and medium arteries and small veins. The CSF lymphocytosis was thought to be due to a meningeal vasculitis. These findings are rare, however.

Any patient who presents with neurological signs and CSF lymphocytosis, with auricular or ocular inflammation, should be considered to have relapsing polychondritis, as lack of recognition of the association may lead to a delay in treatment and a poorer prognosis.

It is known that involvement of the tracheobronchial tree is a sign of poor prognosis and is the cause of death in up to 50% of cases (McAdam et al, 1976; Kilman, 1978; Neilly et al, 1985; Michet et al, 1986). The chest radiograph findings have been described (Sane et al, 1987; Crockford & Kerr, 1988) and involve narrowing of the trachea, pulmonary consolidation and symptoms of airway obstruction associated with major airways collapse. Flow–volume curves have been used to demonstrate airways obstruction (Mohensifar et al, 1982) and demonstrated obstruction in this case (Fig. 3). The flow–volume loop had appearances typical of emphysema but the normal transfer factor was against this diagnosis.

The CT demonstration of respiratory tract involvement has not been widely reported. Findings include involvement of the laryngeal cartilages (Casselman et al, 1988), narrowing of major airways and involvement of the nasal cartilages (Mendelson et al, 1985) and irregularity of the tracheal wall (Booth et al, 1989). The CT scan in this case demonstrated irregularity of the tracheal wall during inspiration and marked collapse of the major airways during expiration. As most CT scans are performed on inspiration, only subtle irregularity of the tracheal wall may be present and may be missed. It is recommended that CT scans for suspected cases of major airway involvement be performed in both inspiration and expiration, for at least selected slices covering the major airways, to assess respiratory changes in calibre of the tracheobronchial tree.

Acknowledgments

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Thorium dioxide, forgotten but not gone

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Keywords: Thorotrast, Liver disease, Radiology

The recent report edited by Taylor et al (1989) reminds us of the continuing risk of morbidity in patients exposed to thorium. We present three cases, with hepatic sequelae, in which the radiological diagnosis was missed on initial presentation. They illustrate the need to be alert to the possibility of Thorotrast toxicity.

Thorotrast, a 25% colloidal solution of thorium dioxide, was a widely used contrast medium from 1928 (Blühbaum et al, 1928) until 1955, when its use was abandoned following a report (MacMahon et al, 1947) of hepatic angiosarcoma associated with exposure to Thorotrast and concern about the long term effects of internal irradiation.

Case reports

Case 1

A 69-year-old female was admitted in 1989 for investigation of malaise, right hypochondrial pain and anorexia. She had had a cholecystectomy 10 years previously at which abnormal liver texture was noted. A liver biopsy revealed cirrhosis. Examination was normal apart from tender, non-pulsatile hepatomegaly. Liver function revealed a markedly elevated alkaline phosphatase and gamma glutamyl transferase. The alpha-fetoprotein (AFP) was not raised. An abdominal X ray (Fig. 1) revealed metallic opacities in the spleen, periphery of the liver and coeliac axis lymph nodes. Abdominal ultrasound showed the liver to be enlarged with increased echogenicity. The spleen was noted to be very small. Further history revealed that the patient had received Thorotrast in 1938 during investigation of a "kidney problem".

A repeat liver biopsy showed multiple deposits of refractile brown material consistent with Thorotrast. There was macronodular cirrhosis with marked periductal fibrosis. No malignancy was seen. Review of the previous biopsy also showed Thorotrast particles and cirrhosis. She was treated with prednisolone on which her general condition subjectively improved with a corresponding improvement in her liver function tests.

Case 2

A 62-year-old man presented as an outpatient in 1979 with a 4 month history of continuous "gnawing" epigastric pain associated with mild anorexia and 3.5 kg weight loss over the preceding 2 months. On examination he had an enlarged liver, visible as an epigastric mass. In 1934 he underwent repair of a right femoral artery aneurysm following a gunshot wound. An angiogram was performed as part of the investigation.

An abdominal radiograph revealed a typical pattern of Thorotrast deposition. An isotope liver scan demonstrated a large area of decreased uptake in the right lobe of the liver. A liver biopsy revealed cholangiocarcinoma, marked fibrosis and deposits of Thorotrast. Whole body gamma spectroscopy demonstrated the typical emission pattern of thorium. Despite chemotherapy his condition steadily deteriorated and he died 3 months later.

Case 3

A 69-year-old man was referred from his general practitioner, in 1989, with "flu-like" symptoms and a palpable liver.

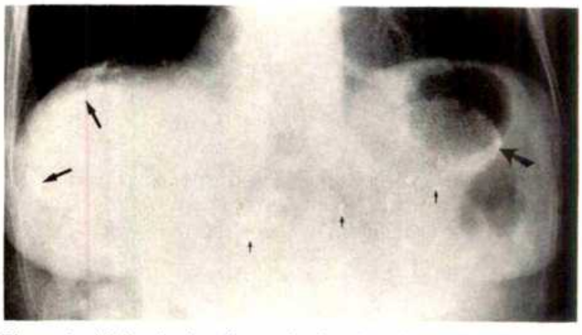

Figure 1. Abdominal radiograph showing the typical distribution of Thorotrast in the liver capsule (large straight arrows), spleen (note punctate distribution) (curved arrow) and para-pancreatic lymph nodes (small straight arrows).

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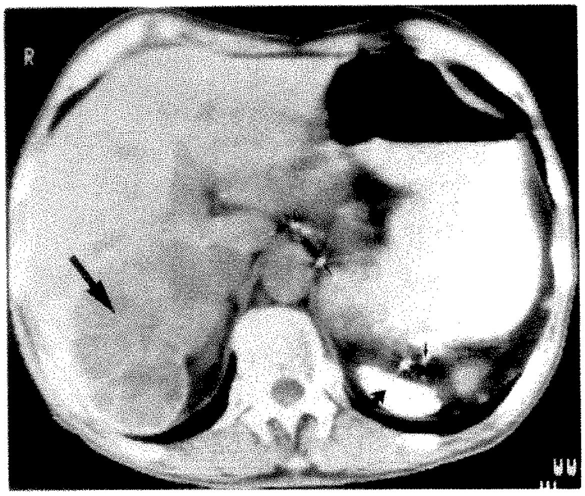

Figure 2. Abdominal CT scan showing a large area of low attenuation in the right lobe of the liver (large straight arrow). Metallic deposits of Thorotrast are seen in the spleen (curved arrow) and peripancreatic lymph nodes (small arrows).

A chest radiograph revealed Thorotrast deposition in the liver and spleen. In 1935 he had undergone carotid angiography during the investigation of migraine. Biochemical and haematological investigations were normal but the AFP was elevated massively.

Ultrasound revealed a 10 cm echogenic mass in the right lobe of the liver and no other abnormality. Computed tomography (CT) (Fig. 2) revealed a large low attenuation lesion in the right lobe of the liver. Thorotrast deposition was noted in the periphery of the right lobe and in the coeliac axis lymph nodes. The spleen was shrunken and full of Thorotrast. He was offered partial hepatectomy for his presumed hepatocellular carcinoma but declined this and has remained well apart from some upper abdominal pain.

Discussion

Thorium is radioactive and, owing to retention in the reticuloendothelial system, has a biological half-life of 200–400 years (Ito et al, 1988). 90% of the emitted radiation is high linear energy transfer (LET) α-particles (Kojiro et al, 1982). The typical dose rate to the liver and spleen is 0.3 Gy/year (Looney, 1960).

Thorotrast is inhomogeneously distributed in the body, 60% is in the liver, 19% in the spleen. The remainder is found mainly in bone marrow (21%) and the para-pancreatic lymph nodes (Ishikawa et al, 1989). This results in the characteristic X ray appearance with diffusely scattered opacities in the liver, spleen and porta hepatis (Gondos, 1973). The abdominal X ray is almost pathognomonic (Velasquez et al, 1985). Where doubt exists the diagnosis is confirmed by total body gamma radiation counting (as in our second case) or by autoradiographic studies of a biopsy specimen.

The formation of aggregates of Thorotrast in the liver in the subcapsular and peri-portal regions results in wide ranges in the local radiation dose which has been estimated to vary from 0·4 μGy to 20 Gy/year (Kaul et al, 1979; Dalheimer & Kaul, 1989). The amount of thorium deposited in the liver can be estimated from the Hounsfield number on abdominal CT scanning (Miyajima et al, 1985). The presence ot Thorotrast induces local fibrosis and hepatocyte necrosis which develops into cirrhosis (Scully et al, 1981). The carcinogenicity is due to local radiation damage (Spiethoff et al, 1989).

Exposure to Thorotrast is associated with decreased life expectancy. Several large studies (Janower et al, 1972; Da Silva Horta et al, 1974; Cayolla da Motta, 1979; Mays, 1979) have shown that there is excess mortality due to liver cirrhosis and malignant disease particularly hepatic cancers (occurring in up to 10% of cases of prolonged exposure) and leukaemias. Cholangiocarcinoma and hepatic angiosarcoma account for 40% each, with the remainder being hepatocellular carcinoma (16%) and unspecified or dual cell type (Kojiro & Ito, 1989). The latent period for the development of hepatic fibrosis is over 15 years and for liver tumours greater than 25 years (Da Silva Horta et al, 1965). Interestingly, the incidence of hepatocellular cancer and hepatic angiosarcoma is increasing whilst cholangiocarcinoma appears to be on the decline (Falk, et al, 1979; Mori et al, 1989).

Thorotrast will continue to cause disease until the end of this century and beyond; however, the incidence of Thorotrast related disease will fall as the number of survivors diminishes. Thorotrast should be considered as a possible cause for liver disease in any patient with a history of angiography up to the mid 1950s. It is important for clinicians, radiologists and pathologists to remain alert to the diagnosis and to be aware of the long term complications of Thorotrast exposure. Any patient known to have been exposed to Thorotrast should be followed-up for life as only early detection of hepatic malignancy will allow effective treatment. All cases should be documented fully in order to increase our knowledge of the consequences of long term exposure to an internal radiation source.

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Radiological manifestation of elastofibroma: a case report and review of the literature

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Keywords: Elastofibroma, CT, Rib fracture, Subscapular, Chest wall tumour

Elastofibroma is a very rare benign tumour of connective tissue, whose features are distinguished by the presence of abundant elastinophilic polymorphic structures and characteristic location. The lesion usually appears in elderly women (50–80 years) characteristically arising from connective tissue in the subscapular region. There are few reports of elastofibroma in the radiological literature (Berthoty et al, 1986; Marin et al, 1987).

We report a case of elastofibroma dorsi presenting with chest radiographic abnormalities and its radiological manifestation is reviewed.

Case report

An 84-year-old Japanese female with no significant medical history was referred to hospital for evaluation of an abnormal chest X ray and a feeling of fullness in the upper abdomen. 6 months earlier she began to experience an occasional feeling of fullness in the upper abdomen. Initial evaluation revealed a

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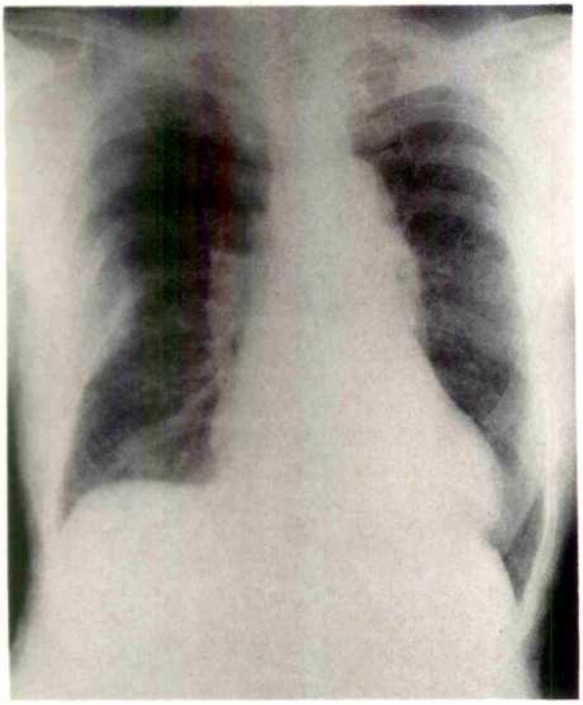

Figure 1. Chest radiograph showing a mass with indistinct upper margins in the right mid zone and fractures of the sixth and seventh ribs.

gastric polyp, 1.5 × 1.5 cm in diameter, and a mass on the chest radiograph. The polyp was biopsied and histologic examination showed no malignancy. On physical examination, the right scapula was displaced slightly, both laterally and upwardly, and a non-tender hard mass was apparent beneath it. The mass was obvious when the patient raised her arms and rotated them anteriorly but was not adherent to the overlying skin. She had no perisubscapular pain, discomfort, or restriction of movement. She had noticed a swelling at that site 5 years earlier and although the mass had increased in size, it was otherwise unremarkable. There was no lymph node enlargement and otherwise the physical examination was normal. Laboratory studies were also normal. The chest radiograph revealed an opacity with indistinct upper margin in the right upper zone and fractures of the sixth and seventh ribs (Fig. 1). A computed tomographic (CT) scan of the chest was performed, and this confirmed an inhomogeneous ill-defined mass located in the subscapular region (Fig. 2) corresponding in position to the mass seen on the chest radiograph. It clearly displaced the right scapula. Tru-cut biopsy of the mass demonstrated elastofibroma (Fig. 3).

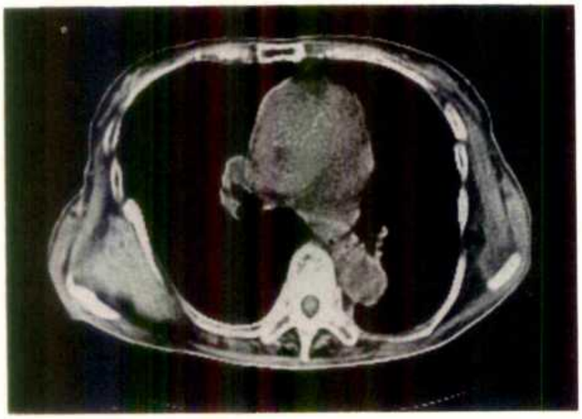

Figure 2. CT scan of the chest showing an ill-defined inhomogeneous mass located in the subscapular lesion.

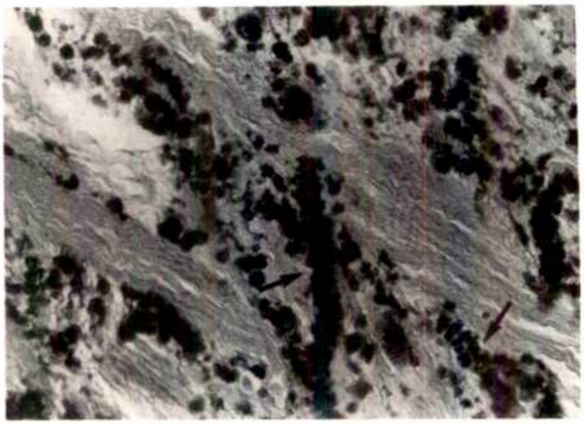

Figure 3. Weigert's elastic stain showing numerous globular and a string of bead-like elastic materials mingling with collagen. Note elastinophilic fibres with a central dark core and grey periphery (arrow).

Discussion

Elastofibroma was first described by Järvi and Saxen (1961). Subsequently, there have been no more than 300 cases in the literature, consisting mainly of sporadic individual case reports. A review of the literature up to 1986 comprising 79 patients was reported by Wening et al (1986). Elastofibroma is a rare fibroproliferative benign lesion of uncertain cause, which usually arises in the subscapular region. Bilateral lesions are common and they may occur asynchronously (Järvi et al, 1969; Nagamine et al, 1982). Other sites of occurrence are uncommon, including the infraolecranon area (Nagamine et al, 1982), the deltoid muscle (Mirra et al, 1974), the ischial tuberosity (Waisman & Smith, 1968), the greater trochanter (Barr, 1966), the intraspinal space (Prete et al, 1983), the axilla (Deutsh, 1974), the greater omentum (Tsutsumi et al, 1985), the orbital area (Austin et al, 1983) and the foot (Cross et al, 1984). In addition, a gastric elastofibroma in association with a subscapular lesion has been reported (Enjoji et al, 1985). A gastric polyp was found in our case, but histological examination of the biopsied specimen did not identify elastinophilic material.

The typical microscopic appearance of the lesion has been well described and is composed of bundles of collagen and elastic fibres. Elastin stains, such as with Verhoeff's and Weigert's, demonstrate the elastic substances in the lesion to be a string of bead-like or necklace-like arrangement, with a central darker stained core and grey periphery. With hematoxylin and eosin

Table I. Summary of the reports of radiographic findings in elastofibroma dorsi (1961 ~)

References	Number of cases	Site	Findings of chest X-ray film and/or CT scans
Deutsch, 1974	1	right	Chest X-ray film: peripheral shadow involving the pleura
Scapinelli et al, 1982	1	right	Chest X-ray film: badly-defined shadow, only slightly more opaque than the surrounding soft tissue
Nagamine et al, 1982	170	bilateral (112/170, 65.9%), right (35/170, 20.6%), left (22/170, 12.9%)	Chest X-ray film: a soft tumour seen over the ribs in the subscapular region
Berthoty et al, 1986	1	bilateral	Chest X-ray film: normal CT scan: subscapular poorly defined non-homogeneous mass with irregular linear low-density streaking
Marin et al, 1987	2	right right	Chest X-ray film: (patient 1) normal (patient 2) a vague opacity extending 8 cm inferior to the inferior angle of the scapula CT scan: (patient 1) a subscapular soft-tissue-density mass without clear marginal definition (Patient 2) an inhomogeneous soft-tissue-density mass elevating the scapula from the posterior chest wall Margins of the mass varied between poorly demarcated and partially well demarcated

staining, these structures stain eosinophilically. Figure 3 is a photomicrograph of the present subscapular lesion using Weigert's stain. The findings were typical of elastofibroma.

Chronic microtrauma and occupational stress have been implicated in the pathogenesis of elastofibroma, but the relationship has not been definitely established (Järvi et al, 1969). Our patient had no occupational history of heavy manual labour.

For this report, we also carried out a search of the radiological literature since the first description by Järvi and Saxen (1961). We were able to review the radiological appearances of individual cases of elastofibroma in five different publications (Table I). Marin et al (1987) reported a case of elastofibroma whose plain chest radiograph showed an ill-defined opacity projected over the lower zone. In our case, the chest radiograph showed a mass overlying the ribs with an indistinct upper margin in the right mid-zone and with associated fractures of the sixth and seventh ribs. Elastofibroma is usually found in the lower subscapular space deep to the rhomboids and latissimus dorsi muscles, and is frequently firmly fixed to the posterior thoracic cage in the region of the sixth to eighth rib (Stemmermann & Stout, 1962; Järvi et al, 1969). Elastofibroma has no capsule and usually infiltrates surrounding tissues, thus mimicking a malignant neoplasm. On plain chest radiography, elastofibroma may be associated with rib fracture. Thoracic CT is useful in the diagnosis of elastofibroma and our search reveals only two reports of three patients describing the CT features of elastofibroma (Table I). CT can readily show extension of the mass into the chest wall and ribs, when the mass may be shown pushing the ribs inwards and, presumably, resulting in rib fracture due to the resultant deformity rather than direct invasion. Differential diagnosis in patients with subscapular tumour includes liposarcoma (Wilinsky et al, 1984), fibromatosis (Campbell et al, 1983) and malignant fibrous histiocytoma (Westreich & Yeshua, 1989). The radiological discrimination between elastofibroma and other mesenchymal malignancy is difficult and needle biopsy is recommended even if the radiological findings are typical of elastofibroma.

Deutsh (1974) reported a case showing a good response of elastofibroma to radiotherapy treatment. However, no treatment is necessary in the asymptomatic patient because the lesion is benign. The treatment of choice for symptomatic elastofibroma is local excision and recurrence has not been reported after surgical excision. As our patient was virtually asymptomatic excision was not performed.

Elastofibroma dorsi describes the findings in this patient because of its typical site, but it should be noted that this condition is not exclusively confined to the subscapular region.

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Case of the month

A leaking laparoscopy wound

By F. Regan, MRCP and M. E. Crofton, MRCP, FRCR

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(*Received May 1990*)

A 34-year-old Bahrainian woman presented to the Accident and Emergency Department complaining of fluid leaking from a recent laparoscopy scar. She spoke very little English so no further history was available. Examination of the abdomen was unremarkable. She was referred for an ultrasound examination of the abdomen to exclude an intra-abdominal collection or urinoma.

A midline sagittal scan of the pelvis and a parasagittal scan to the left are shown (Figs 1 & 2). What is the diagnosis? What were the likely indications for the laparoscopy?

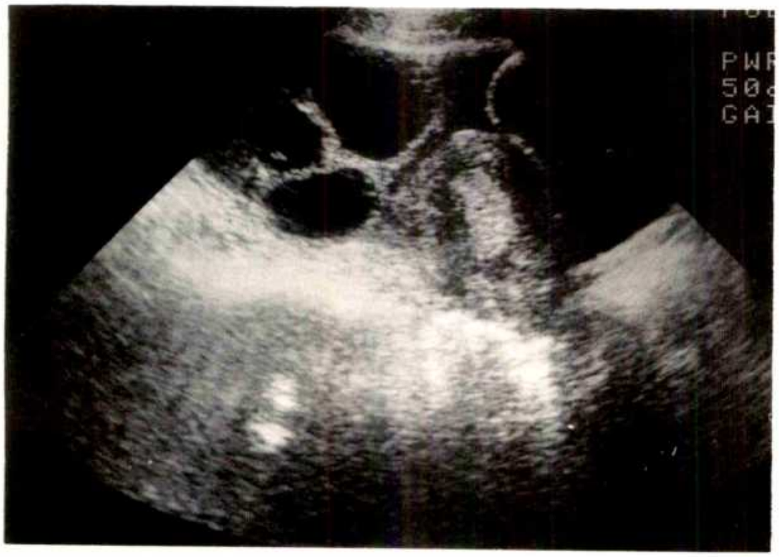

Figure 1. Parasagittal scan of the pelvis showing a thickened endometrium.

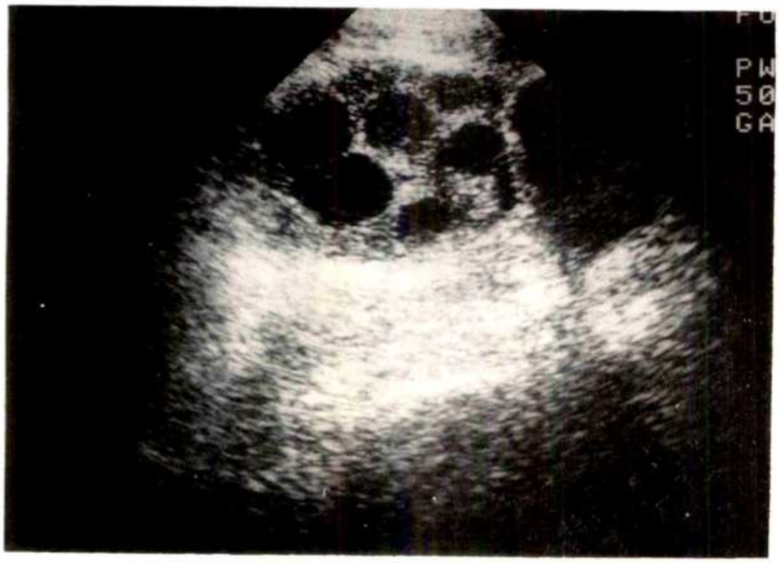

Figure 2. Parasagittal scan to the left showing an enlarged ovary with multiple cysts.

The ultrasound examination revealed a moderate amount of ascites, later confirmed to be the source of the leaking fluid. The uterus was normal in size but had a very thickened endometrial echo (16–18 mm antero-posterior diameter). Both ovaries were enlarged (8 × 4 cm approximately) and contained multiple 1.5–2.0 cm cysts. These appearances are those of Ovarian Hyperstimulation Syndrome (OHSS). It was subsequently learnt that she had undergone ovulation induction therapy prior to *in vitro* fertilization. Laparoscopic egg collection had been performed in Belgium 2 days before presentation, but unfortunately none of the retrieved oocytes had fertilized so no embryos had been returned to her uterus. The patient insisted on returning to Bahrain following her diagnosis and as far as we are aware made an uneventful recovery.

Discussion

The OHSS has frequently been described in the literature since Gemzell first described successful induction of ovulation and pregnancy in humans in 1958. The syndrome is usually of minimal consequence but can be a potentially life threatening condition, characterized by enlarged ovaries containing multiple cysts and extravascular fluid collections, ascites and pleural effusions. Exceptionally, pleural effusions may occur without an increase in ovarian size. There is haemoconcentration and in severe cases circulatory collapse and various coagulation disorders including disseminated intravascular coagulation can occur. Abnormally high levels of oestrogen are found in the patients serum, urine and follicular fluid and there are raised plasma levels of progesterone, 17-hydroxyprogesterone and testosterone. It is usually seen in association with various ovulation induction regimes (to treat ovarian dysfunction in infertility or to induce superovulation prior to *in vitro* fertilization), but has been reported in association with hydatidiform moles and multiple pregnancies occurring without the aid of ovulation inducing agents.

The severe form of the disease is rare with a reported incidence of 0.4–4% of patients on ovulation induction therapy. The milder form is much commoner (reported rates vary from 3–80%) and many cases undoubtedly go unrecognized.

The pathogenesis and aetiology of the syndrome are unclear. There is thought to be a sudden increase in the permeability of the ovarian vessels and the fact that the extravascular fluid collections are transudates supports this. Crooke et al (1963) found that high follicle stimulating hormone (FSH)/Luteinizing hormone (LH) ratios resulted in a lower incidence of OHSS, but subsequently this could not be confirmed. Schenker and Weinstein (1978) showed the dose of gonadotrophins was significant but that the critical dose varied enormously between individuals.

Histamine release blocking agents and prostaglandin inhibitors have been tried with variable success, but treatment of the condition is mainly supportive with correction of any fluid and electrolyte imbalance. It usually resolves spontaneously in 7–10 days. Primarily effort should be directed at preventing development of the syndrome by careful monitoring of all ovulation induction regimes and removal of the stimulating agent should the condition arise.

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Keywords: Ovarian hyperstimulation syndrome, Ovarian enlargement

1991, *The British Journal of Radiology*, *64*, *1075–1077*

Correspondence

(The Editors do not hold themselves responsible for opinions expressed by correspondents)

Nitrous oxide — radiosensitizer or radioprotector?

The Editor—Sir,

As part of a wider study of the radiobiological effects of narcotic gas mixtures (Conere, 1989) the possible radiation protection of Chinese hamster ovary cells (CHO) using a 99% nitrous oxide: 1 ± 0.05% oxygen gas mixture has been investigated. This gas mixture was used in the expectation that the narcotic component in the mixture might displace oxygen from sites within the cells where oxygen is required in order to confer oxygen dependent radiosensitivity.

1% was used in the gas mixtures on the basis that further displacement of oxygen in line with the Ebert et al hypothesis (1958) would be readily detectable given the shape of the Alper and Howard-Flanders (1956) hyperbolic response curve relating radiosensitivity to oxygen concentration. This also avoided any artefacts associated with a small degree of oxygen contamination (*e.g.* from plastic culture vessels) when complete anoxia is attempted.

The data were fitted to dose–response curves using the linear-quadratic model. There was no significant difference between the survival curves for cells irradiated in air or in 99% nitrous oxide: 1% oxygen, thus a single curve has been fitted to those data for comparison with the curve for cells irradiated in 99% inert gas: 1% oxygen (Fig. 1). The two curves are significantly different (alpha values of 0.223 ± 0.005 and 0.207 ± 0.003 Gy^{-1} and beta values of 0.0356 ± 0.0006 and 0.0226 ± 0.0005 Gy^{-1} for the air/nitrous oxide and inert gas data, respectively). The results indicate no protective effect of using nitrous oxide. This gas appeared to sensitize as much as air. Such sensitization was seen to be additive to that obtained with 99% inert gas: 1% oxygen.

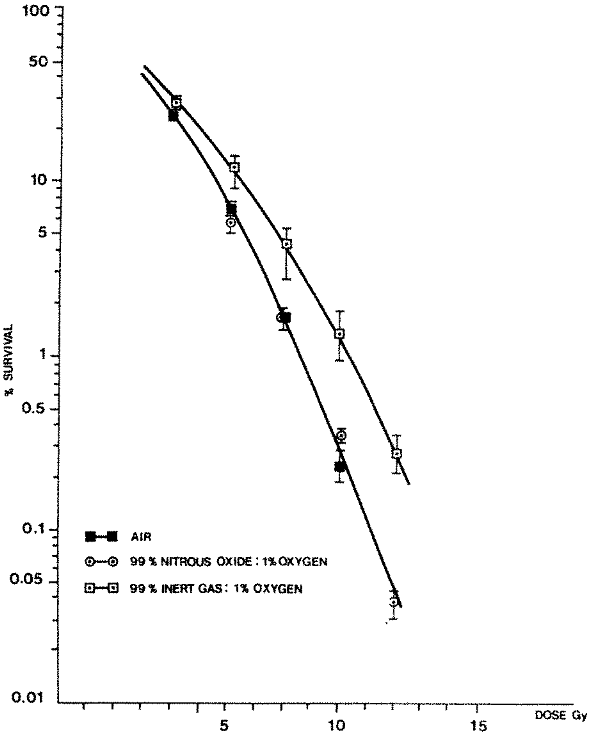

Figure 1. Irradiation cell survival curves for Chinese hamster ovary cells whilst exposed to various gas mixtures. Irradiation was with 212 kV X-rays (half value layer = 0.83 mm copper).

Whilst Ebert and Hornsey (1958) demonstrated major radioprotection using an 80% nitrous oxide: 20% oxygen gas mixture, the present findings indicate that the Ebert et al hypothesis (1958) does not have general application. This may be a consequence of different test systems, biological endpoints used and also irradiation conditions. The present work and that by Roots et al (1982) are, to our knowledge, the only studies that indicate sensitization of mammalian cells *in vitro* by nitrous oxide. This agreement was obtained using very different experimental procedures with a consensus of 19% sensitization by Roots and 26% by ourselves (at the 0.3% survival level) with respect to nitrogen and 99% nitrogen: 1% oxygen gassing, respectively. Such findings might balance the present evidence concerning the radiosensitivity of mammalian cells in the presence of nitrous oxide.

Ewing et al (1986) found that the amount of sensitization of V79 Chinese hamster cells by oxygen in an oxygen/nitrogen mixture, did not change when the nitrogen was replaced by nitrous oxide. This contrasts with our present results. Michaels et al (1983) did not find any direct evidence of nitrous oxide sensitization of CHO cells. However, in the presence of the OH• radical scavenger 3M DMSO, 20% enhanced sensitization was obtained in nitrous oxide saturated conditions compared with irradiation under nitrogen saturated conditions.

In conclusion, the radiation response of mammalian systems to nitrous oxide and even to anaesthetic/narcotic agents in general, has in our opinion yet to be resolved, with possible consequences for present and perhaps future clinical treatment strategies (Conere et al, 1986; Conere, 1987).

Acknowledgments

We wish to acknowledge the helpful suggestions and comments of Dr O. C. A. Scott, The Richard Dimbleby Department of St Thomas' Hospital and thank Mr John Saunders and his staff from the Medical Physics Department for providing radiation dose calibrations.

We also thank Professor W. S. Lowry, Department of Oncology, The Queen's University, Belfast, for his encouragement and the Ulster Cancer Foundation and Friends of Montgomery House for their financial support.

Yours, etc.,

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Percutaneous femoral artery puncture: practice and anatomy

The EDITOR—SIR,

I read with interest Dr Hartnell's opinion that fluoroscopy is hardly ever warranted in puncturing the femoral artery (Grier & Hartnell, 1991). Perhaps our patient populations are different, but not infrequently I have to puncture a barely palpable, or indeed a non-palpable artery shown to have flow on non-invasive imaging. My experience is also of thousands of punctures, the majority in severly atherosclerotic vessels. While translumbar, axillary or brachial punctures are then usually indicated, my practice is to attempt a retrograde examination as I have developed faith in the non-invasive assessment that the vessel is open.

I do not understand how fluoroscopy slows down the case throughput, as confirmation of catheter tip placement and a contrast injection for timing purposes both require fluoroscopy. Reliance on arterial backflow and depth of placement of the catheter alone is not optimal angiographic technique in 1991 (Darcy, 1991), however widely this is still practised.

Dr Hartnell missed my point about the usefulness of checking the fluoroscopy unit by actually using it. I assume nothing when performing invasive procedures, and few radiographers actually check the foot-pedal function. I prefer to know that fluoroscopy is available immediately if required. Has Dr Hartnell never been in a vessel with a good backflow where the guidewire will not advance despite manipulation and the use of a floppy tip guidewire? A contrast injection through the needle under fluoroscopy will often clarify the problem without the need for, and risk of, a second puncture.

The detection of vascular calcification is by no means as irrelevant as Dr Hartnell thinks. In difficult punctures tubular or linear calcification can be very useful in locating the vessel exactly, and occasionally in avoiding it if the vein is being sought.

Some of these differences in our respective techniques may be caused by severity of disease of obesity requiring closer attention to the puncture technique, but I doubt it. Neither do I work in lavish facilities under no time pressure, fiddling with fluoroscopy while real work is waiting to be done. My aim is a clean vessel wall puncture on the first attempt, at a safe level along the common femoral artery, with certain knowledge of the position of the catheter tip, assessment of the flow rate with contrast, and selection of a table movement rate which will show all vessels down to and including the feet without the need for a second run. This cannot be done well without fluoroscopy.

Yours etc.,
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(Received April 1991)

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How and why are ultrasonic scanners chosen?

The EDITOR—SIR,

What is it that influences the purchase of ultrasound scanners? We recently conducted a postal survey concerned with this. Our objective was to find out how prospective purchasers obtain the information that enables them to select the equipment that they would like to buy. We did not try to discover what features of equipment design, performance and cost are relevant to equipment selection. It is after all reasonable to suppose that purchasers desire ergonimicably designed equipment that produces good images and is competitively priced.

We sent a questionnaire to 108 colleagues whom we knew to be actively involved in medical ultrasonic diagnosis; there was a 78% response rate (54 radiologists, 30 others). We were thrilled that so many too the trouble to reply and thank them very much.

The questionnaire asked for a score from 0 to 5 to be given for the value of each of a series of possible influences that purchasers might consider, 0 representing least value, 5 the most. These influences included contact with sales people, seeing equipment at commercial exhibitions, taking expert advice and visiting other hospitals to see equipment in use.

Detailed presentation of the results is not appropriate in this letter so we have condensed them to produce a league pie chart of those influences thought to be useful by our respondents (Fig. 1). A very striking, but not unexpected, result is that the most valuable influence is a "hands-on" trial of the equipment. Interestingly, none of the respondents mentioned that advertisements, about which we did not specifically enquire, had any impact.

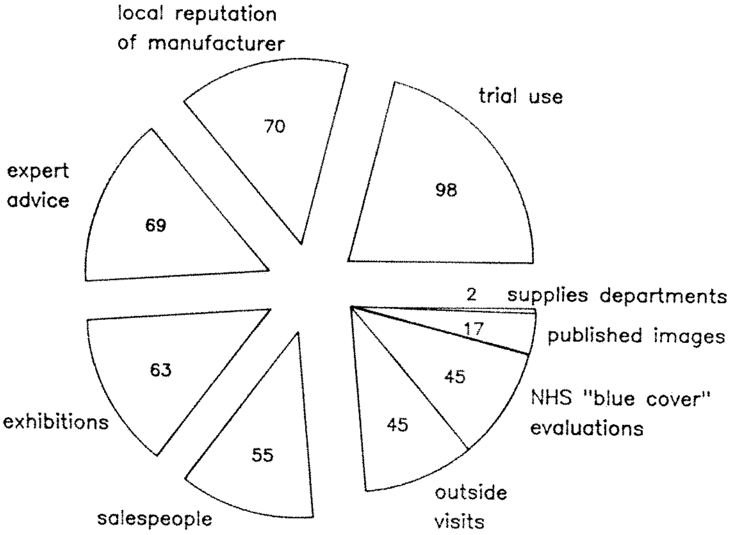

Figure 1. Percentages of respondents who thought that these influences were useful.

Unsurprisingly, the winner of the least helpful category was the hospital supplies department (medical physics departments were volunteered by some as very useful sources of information, naturally). For simplicity, the pie chart is a compilation of all the responses but some interesting observations arise from considering the replies in two groups: "radiologists" and "others". For example, others rated attendance at commercial exhibitions as very valuable while the majority of radiologists called it moderately useful; perhaps this reflects the good time that others experience at exhibitions (of course, radiologists have a good time all the time and so do not notice the change). Another difference in opinion occurs with the semi-official NHS equipment reports (the Ultrasound Equipment Evaluation Project: STD blue cover reports). The majority of radiologists thought that they were of moderate value whereas most of the others considered them of little or no value. Frequent criticisms of these reports were that they tend to be out-of-date when published and are perceived to be of dubious relevance to realistic scanning.

Neither of the groups were much influenced by published images but the radiologists were slightly more affected by both the local reputation of the manufacturer and by advice from experts. For all the other categories there was broad agreement between the groups.

The result of this survey demonstrates that there are five major sources of influence in the choice of ultrasound scanner: a trial period of use; the local reputation of the manufacturer; commercial exhibitions; visits from sales people and advice from experts.

Yours, etc.,
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1991, *The British Journal of Radiology, 64,* 1078–1080

Book reviews

MRI Musculoskeletal System. By Javier Beltran, pp. xi + 344, 1990 (J. B. Lippincott Company, Philadelphia), $79.50.
ISBN 0-397-44644-6

This book is written by Javier Beltran but includes contributions from several of his radiological colleagues and is largely based at the Ohio State University Hospitals.

The first chapter briefly describes the physical principles of magnetic resonance imaging (MRI) and it is followed by eight chapters devoted to individual regions: the temporomandibular joints; shoulder; elbow; hand and wrist; pelvis and hips; knees; ankle and foot and the spine. The last two chapters describe the current application of MRI in musculoskeletal tumours and infections. The layout of each chapter is similar and commences with a discussion on suggested imaging techniques. Although this discussion is particularly applicable to the 1.5 Tesla GE signa unit used to obtain most of the published images, it would in general be applicable to other systems and those operating at lower field strengths. This is followed by a detailed description of the normal anatomy of the region in question. These sections are extensively and clearly illustrated by MRI scans with corresponding line drawings. The last section in each chapter is devoted to documenting pathology. As mention is made of most of the lesions which can be encountered at each site, none of the lesions are discussed in great detail. In certain important areas such as the knee, I feel that the absence of any discussion on the now well-known pitfalls in interpretation of MR images of the knee is a rather important omission. Whilst I appreciate that it is difficult for any textbook to present an accurate account of the current state of understanding of MR images, since it is expanding so rapidly, I feel that in some chapters the descriptions do not fully reflect the available knowledge even at the time of writing. Considerably more is known, for instance, about the MRI appearances in Rotator Cuff disease than is indicated in the text. Conversely, a separate description of the MR appearances of joint effusions, osteoarthritis, haemophilic arthropathy avascular necrosis, rheumatoid arthritis and various other lesions in several different chapters seems largely unnecessary and repetitive.

The intent of this book is to acquaint readers with the common MRI manifestations of musculoskeletal disorders. This aim is achieved and certainly a radiologist in training or a practising radiologist without any prior knowledge of musculoskeletal MRI would find much in it of value. In particular the sections on scanning techniques and normal anatomy are informative. The illustrations are generally of good quality and are well annotated. In addition, the book is not over-priced. However, I do not feel that the text would meet the needs of a practising musculoskeletal radiologist requiring to gain an understanding of the full potential and limitations of MRI in all areas.

C. HERON

MRI of the Musculoskeletal System—A Teaching File. Ed. by Jerrold H. Mink and Andrew L. Deutsch, pp. xv + 607, 1990 (Raven Press, New York), $144.00.
ISBN 0-88167-559-8

This book grew out of a perceived need by the editors for "a comprehensive test on musculoskeletal MR" and the observation that "large major references on MR devote surprisingly little space to the interpretation of musculoskeletal MR images". The editors' aims are well met and the book indeed fills an important need. There is extensive coverage of the conditions in which magnetic resonance imaging (MRI) may be applied including the evaluation of the major joints, spine and musculoskeletal tumours and the application of kinematic MRI.

Each chapter is arranged as a series of case studies in which questions relating to MR images are posed. This is followed by the answer, differential diagnosis and a detailed discussion concerning the clinical entity under consideration, in addition to the appropriate application of other imaging modalities where indicated. This format makes the book both readable and informative, however, it works least well in the chapter devoted to technical considerations. For those with a working knowledge of musculoskeletal MR the seven case studies devoted to this topic will provide little additional information. I believe that readers without such knowledge would benefit from a more cohesive and comprehensive overview.

In general the illustrations are of high quality and are well annotated, although the reader's understanding of the MR appearances in a patient with anterior dislocation of the shoulder will not be assisted by a typographical error resulting in the reversal of one of the MR images. I also feel it is unfortunate that three-dimensional gradient echo imaging of the knee is largely dismissed, since many centres are now employing this technique to considerable advantage in the evaluation of internal derangement. This book is primarily a teaching file of diseases rather than normal appearances and some knowledge of cross sectional anatomy of the musculoskeletal system is assumed. In certain instances it may therefore be necessary to use the book in conjunction with an atlas. References are not included in the text, but there is a comprehensive bibliography at the end of every chapter.

Enormous progress and expansion has taken place in musculoskeletal MR recently and it is therefore pleasing to see a book which is up to date at the time of publication, and gives an accurate account of the current applications of musculoskeletal MR. I can recommend the book for use in all MR units engaged in musculoskeletal imaging and to radiologists and orthopaedic surgeons who wish to acquire detailed knowledge in the field.

C. HERON

Radiation Oncology Radiobiological and Physiological Perspectives. By Hassan K. Awwad, pp. xiii + 682, 1990 (Kluwer Academic Publishers, Dordrecht, The Netherlands), £110.00.
ISBN 0-7923-07836

This is an extremely detailed book, primarily aimed at providing the practising radiotherapist with the radiobiological principles relating to the development of better cancer treatment. However, in addition it would be a valuable text for trainees in radiotherapy and for radiobiologists.

A particularly important section of the book deals with the important problem of normal tissue effects (Part III), because, as the author states in the preface, complication free tumour control is a cardinal principle in modern radiotherapy. Although it is perhaps in a little bit too much detail for the trainee, this book in dealing with this aspect of therapy is greatly superior to others that are frequently recommended, where more emphasis is frequently placed on the cellular aspects of radiobiology.

One of the most helpful features of the book, as an aid to the understanding of the topics raised, was the general format of each chapter. At the beginning of each chapter there was an extended summary giving a good guide to the range of material covered; in general terms these were excellent. The material covered included both clinical and experimental aspects. The source material on which the chapter was based is also listed along with other recommended future reading at the end of each chapter. Again these are arranged in an extremely valuable way, by topic. These reference lists are very up to date and I found very few areas where what could be considered key references were missing.

In a volume of this type one can always find errors and this one is no exception. However, in most instances these were small errors of fact and not interpretation. The figures on pages 144 and 145 have also been transposed in error.

The book has been prepared in camera ready format which is somewhat surprising for such an extensive publication and for this reason alone the price of £110 would appear to be a little high. However, it does provide a detailed and up-to-date overview of many aspects of the radiobiological basis of radiation therapy and should appear on both the shelves of libraries and those of the research orientated specialist.

J. W. HOPEWELL

Head and Neck Oncology Clinical Management. Ed. by A. R. Kagan and J. Miles, pp. vi + 176, 1989 (Pergamon Press, Oxford), £33.50.
ISBN 0-08-034479-8

On first picking up this book I assumed it was the proceedings of a conference, as it contained 20 contributions by different authors on a diverse range of topics. In fact it is a collected series of essays obviously intended to be read by practising head and neck oncologists. The editor states in the introduction that it is hoped the volume will help to show the changing perspective and growth of wisdom with time.

Certainly some of the contributions are largely philosophical. Donald Harrison discusses the merits of some major palliative operations under the heading "Is surgery for the benefit of the patient or the surgeon?"; the question remains largely unanswered. There is an interesting essay on informed consent by Paul Ward of UCLA which shows the difference in both medical and legal practice between UK and USA. His ideals about the time which should be spent with a patient establishing communication are highly desirable but rarely attainable; Dr Ward seems to realize this, saying that it is inevitable that society will eventually decide priorities and ration medical care.

Many other chapters are more practical, dealing with aspects of treatment and rehabilitation. Especially good are two contributions from experts, working in centres, with a vast experience of their subject, B. J. Cummings of Princess Margaret Hospital on juvenile angiofibroma and J. P. Bataini and F. Brunin of Foundation Curie on supraglottic carcinoma. Other chapters are of more variable quality, ranging through such topics as medullary thyroid carcinoma, osteoradionecrosis, mandibular reconstruction and chemotherapy.

The book is well produced and presented with few misprints. The black and white illustrations are of good quality. It is very reasonably priced at £33.50. Those actively engaged in the practice of head and neck oncology will enjoy reading it, but it is not a book likely to be kept on the shelf for reference.

J. M. HENK

Review of Radiology. Ed. by Carl E. Ravin and Cirrelda Cooper, pp. xviii + 339, 1990 (Harcourt Brace Jovanovich Ltd, Kent), £25.00.
ISBN 0-7216-7477-1

This book evolved from a training course run by the Department of Radiology at Duke University Medical Center for residents and qualified radiologists. The text is in note form. There are chapters on each body system and on radionuclide imaging and ultrasound. Radiological features of disease, together with some clinico-pathological information, is interspersed with differential diagnoses of radiological signs in bolder print. There are no radiographs, although some line drawings are present. Generous margins encourage readers to add their own notes.

Not surprisingly, in a multi-author book with an abbreviated text there is some unevenness of style and a certain amount of repetition. For instance, there are detailed percentages of rare conditions in some places, but elsewhere there are some lists which are so terse as to be almost meaningless. The sections on congenital heart disease and the neonatal chest are particularly good. A very complex section on congenital abnormalities within the central nervous system is out of step with the otherwise concise and didactic chapter on the head and neck.

Trainees may find this book a useful adjunct to their preparation for examinations, provided that it is seen as a revisional supplement to more substantial and illustrated reading.

G. H. WHITEHOUSE

Radiology of the Small Intestine. By P. Bret, C. Cuche and G. Schmutz, pp. xvi + 305, 1989 (Springer-Verlag, Berlin), DM 398.
ISBN 2-287-00014-3

This elegant work from France joins a veritable plethora of books on small bowel radiography which have been published in recent years. Amongst these are new books by authors such as Sellink, Antes and Eggeman, Herlinger and Maglinte; so this text joins an already crowded field.

Is it any different? Like those mentioned above, the major emphasis in this volume is the demonstration of small bowel pathology by barium contrast, with reference being made of additional imaging such as computerized tomography, ultrasound etc. The main difference relates to technique. All the above authors are champions of tube studies of the small intestine, whereas it is clear from the illustrations that Bret, Cuche, and Schmutz tend to favour a conventional follow through with graded compression. Does the book suffer as a result? The answer is a resounding no; as they have succeeded in producing a magnificent work which demonstrates that although techniques may vary, it is attention to detail which counts.

The book is written along conventional lines with opening chapters on clinical and technical aspects including the performance of small bowel enemas. It then moves into pathology affecting the small bowel. This is very comprehensive and reference is made of every conceivable disease affecting the small bowel. It is beautifully illustrated throughout and the references are full and up to date, although not cited individually in the text.

I can find little to fault here as this can be used as a major reference work to help resolve the dilemma case, as well as being a delight to both read and browse through. The major problem would relate to price which would be daunting for the individual radiologist, except for the keenest small bowel enthusiast. However, there is little doubt that this book would be a very valuable addition to any departmental library and as such it can be strongly recommended.

A. FREEMAN

The Radiology of Skeletal Disorders Exercises in Diagnosis, Volumes 1–4. By R. O. Murray, H. S. Jacobson and D. J. Stoker, 1990 (Churchill Livingstone, Edinburgh).
ISBN 0–443–019800

This is the latest, and greatest, edition of a major work which broke new ground when first published as a single volume in 1971. Overall, these three volumes contain only slightly more pages than did the second edition but the work has been considerably rewritten and updated. In addition, there are new chapters on the use in musculoskeletal disease of computerized tomography (CT), magnetic resonance imaging (MRI) and ultrasonography, as well as radionuclide scanning. The late Bill Stripp's excellent chapter on radiography remains.

The format of the book is unchanged—'exercises' with radiographs and a short accompanying clinical history are used to illustrate specific diseases. The answers are preceded by clinical, radiological and pathological descriptions of the disease entity and are followed by references which have been updated since the last edition. The individual chapters follow traditional classifications of disease but 'lateral thinking' occurs, for example, the exercise on the traumatized child syndrome is followed by a question on osteogenesis imperfecta, and another film of hyperplastic callus in paraplegia.

The text is easy to read, flowing and descriptive. The book is differently organized to the other major orthopaedic radiology texts. In a sense it is not a reference work, or rather it is more than a reference work alone. It is an active, rather than passive, education. The student has to become personally involved—to put in as well as take out. This approach makes the book more difficult to use in a diagnostic situation than a conventional text, but it can be more fun.

The illustrations are of high quality and come from two unique radiological collections which can hardly be equalled. The book is worthwhile buying for these alone.

A personal tribute should be paid to the authors, especially to the senior contributors Ronald Murray and Harold Jacobson. They have given much to radiology at national and international levels and have taught with devotion to their students, patients and discipline. This unique work is a tribute to their skill and dedication.

PETER RENTON

Exercises in Radiological Diagnosis Cervical Spine: Tricks and Traps. By J. F. Bonneville and F. Cattin, pp. vii + 124, 1990 (Springer Verlag, Berlin), DM 35.
ISBN 3–540–17683–7

This book deals with a plain film assessment of the cervical spine and as the name implies, it concentrates on traps and useful hints in interpretation. The reader's knowledge of the anatomy, pathology and basic radiology of this region is assumed and indeed necessary to fully appreciate its content. The book consists of 60 example cases. In most questions are asked of the reader, the answers to which are then carefully explained, often with the aid of line drawings. The latter are particularly helpful as the radiographic abnormalities are not always clearly demonstrated. The illustrations are, on the whole, of a high standard. There are several 3-D computed tomography (CT) scans included which are a useful aid for comprehension. There are no colour illustrations.

This is the sort of book that can be read cover to cover at one sitting, or could just as easily be appreciated taking a few cases at a time. All practitioners involved with the interpretation of cervical spine radiographs will find this book useful. By its very nature this book will not become outdated. This book would be a useful addition to any radiology or orthopaedic library.

C. E. WILLIAMS

BIR Bulletin

Honorary Editor, BIR Bulletin: D. Rickards, LRCP, MRCS, FFR(D)SA, FRCR
Please address all correspondence to: Honorary Editor, BIR Bulletin, The British Institute of Radiology,
36 Portland Place, London W1N 4AT

The British Institute of Radiology is not responsible for opinions expressed in the BIR Bulletin

The EEC and the EANM: A Forum for Information and Action

Professor Ell invited a number of senior members of the European Community Research Programmes to inform an invited group of EANM committee members about the structure and organization of the EC research programmes.

I believe that the meeting was very successful with useful information disseminated with a constructive dialogue between the speakers and the audience. It would be impertinent of me to attempt to condense the seven papers into a precise paraphrase of their content. However, my general impressions are as follows.

The overall purpose of the Commission of European Communities is to further the advancement of all its member states primary by means of collaboration and cooperation. Community research activities carried out within the framework programme are managed by a number of different Directorates-General (DG). The ones most relevant to the health service field are:

DG XII	Science, Research and Development (including overall science and technology policy).
DG XIII	Telecommunications, Information Idustries and Innovation.
DG V	Human Capital and Mobility.

The overall strategies of the framework are agreed at ministerial level. The new framework programme (1990–94) has three main areas — enabling technologies, management of natural resources and management of intellectual resources. It will have an overall budget of 5700 MECU and will be split into 15 specific research programmes.

The DG's after consultation with experts in particular fields, further subdivide the general aims into more specific tasks. At this point calls for proposals are made in the EC Official Journal as an invitation for potential participants in a community research programme to submit project proposals. Deadlines are set and rigidly adhered to.

All proposals must include participants from at least two community states and, for DG XIII, must include at least one industrial firm. It is obvious that the proposals must be carefully targeted at identified tasks.

The EC research programmes are not meant to fund the basic research but to enable workers within the programme to meet on a regular basis. It is imperative that any proposals realistically incorporate travel and subsidence allowances and that at least 50% of the total cost of the proposal will have to be met from other resources. However this seems to be taken on trust.

The proposals are examined in depth by invited experts and finally some are accepted. Certain proposals may be similar and combined. The number of proposals accepted must depend on the total amount of money available — which in turn relates to the amount of money each member state is prepared to allocate. In the medical and health research programme it was stated that 60 from 600 applicants were accepted.

It might be of interest to note the prerequisite conditions for funding in the medical and health research programme (Coordination Budget 1987–1991 – 65 MECU).

(1) The proposal (Conserted Action — CA) must aim at having an "added value". This means in particular that the overall scientific output should exceed the sum of the end results of the individual activity, and/or that output cannot be achieved without such a CA taking place.

(2) Number of participants: groups from at least three countries must take part in a CA, but a total of six or more is common and, indeed, many CAs involve all member states plus other participating countries. The smallest CA has five groups, but the normal range is from 10 to 40 groups.

(3) The subject-field of a CA must come within the content of the EC medical and health research programme.

(4) The appraisal of the proposals for concerted actions by the selection committees is based particularly on the following elements: scientific/clinical merit; European dimension; exploitation of research results; managerial aspects

In any project involving a multinational content and multinational funding, managerial control is of prime importance. This was particularly emphasized in the AIM programme (advanced information in medicine DG XIII) which is primarily targeted at R & D between Universities and Research Institutes, Industry and Hospitals. Again "added value" is paramount but in this case "leading to awareness creation on a European scale of the market opportunities and macro-economic benefits which will accompany the development of an advanced health care telematics infrastructure in Europe." After proposals have been submitted and accepted, formal contracts are agreed between the AIM secretariate and the proposed consortium. This includes regular and detailed report submissions, regular meetings at Brussels between project leaders of each consortium, and a final evaluation by an external accessor.

Dr Britton, as the project leader of such a consortium, reported that over a 1 year period he had produced 49 reports containing a total of 628 pages and he or another member of the consortium had to attend meetings in Brussels every 6 weeks. He quoted from a remark of a senior EC member "People think that Brussels is a goldmine, in fact it is a papermill." Nevertheless the consortium was actively engaged in a new proposal to continue the project after the present funded programme finished. However a scientific officer from DG XII was at pains to point out that the medical and health research programme was not so environmentally destructive but agreed that the principles were similar.

At the more specific level, an acting adviser spoke on the EEC and radiopharmaceuticals and stated that radiopharmaceuticals will be treated exactly as any other pharmaceutical and that registration would be necessary by January 1992. Guidelines, available since December 1990, would be issued to member states but registration is solely the responsibility of the National Authorities. Therefore, any pressure groups must work through their National Authority to the EC. National Authorities may need help at the expert level and that support in the fields of clinical trials, appropriate specialised training and pharmacovigilance was to be encouraged. The problems of the limited radiopharmaceutical market and of long established non-licenced products was accepted but no clear solution seemed to have been found. An EANM member from Germany pointed out that their Pharmaceutical Licencing legislation included a mechanism for treating products of limited daily production as a special case. Guidelines for the legislation of the use of monoclonal antibodies are still under discussion.

An area of opportunity which may not have occurred to some is in teaching and training. This can apply to radiation protection and to schools such as the one organised for 1991 on Nuclear Medicine. The 1984 directive on protection of the patient includes the need for training and education at all levels including General Practitioners and final year medical students and a common basis is required throughout the Community. Most of the radiation protection guidelines are based on ICRP recommendations and the new 1990 recommendations will require action and modifications to existing guidelines.

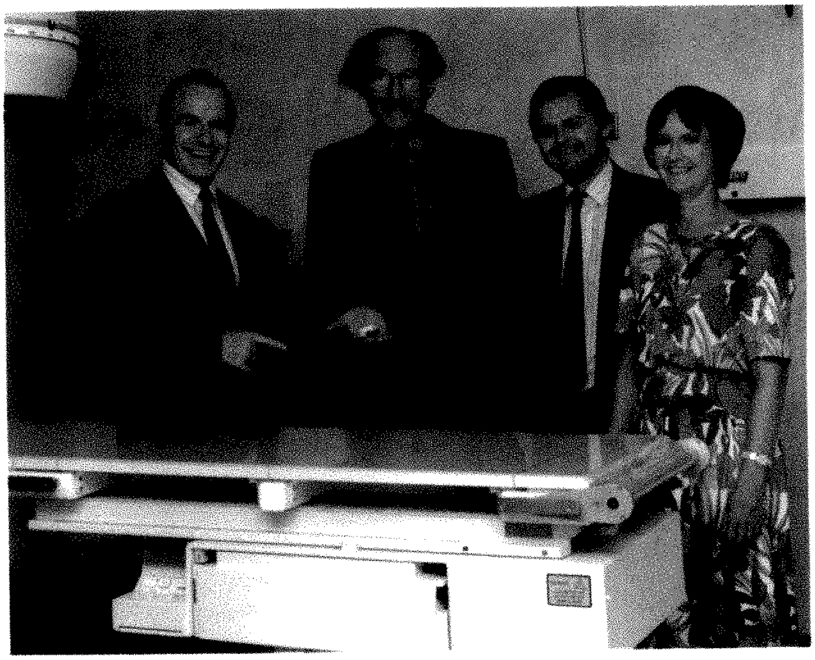
Within DG XII is a radiation protection programme which includes a project dealing with the assessment of patient dose from radiopharmaceuticals. The recommendations within ICRP 1990 on new risk restimates and the possibility of mental retardation require the collection of detailed information on radiopharmaceutical biokinetics and dosimetry, particularly on the new born and young children. It was pointed out that one of the important features of the concerted action mechanism is that the possibility to join an ongoing activity always remains open so that groups working in this field are likely to be welcomed. Informaiton on $^{99}\text{Tc}^{m}$-HMPAO, MDP and DTPA in children would be particularly useful.

In conclusion, it would appear that seeking support from the EC is not a trivial pursuit and must be undertaken with considerable enthusiasm and dedication and a passion for Brussels airport. It does however provide the opportunity to meet and collaborate with colleagues from other countries and enable progress to be make in areas impossible at a national level.

A. H. Smith

Product News

Two more Philips Linear Accelerators for Mount Vernon



Mr Roy Jones, Managing Director of Philips Medical Systems,(L) handed over two SLh75/5 Linacs to Professor Stanley Dische (CL) at an official ceremony. Also shown are Mr Steven Ramsden, General Manager (CR) and Ms Meg Macdonald, Supt. Radiographer (R).

There are a total of five Linear Accelerators at Mount Vernon, all manufactured by Philips. Mount Vernon is the first site to be equipped with the latest version of the SL75/5 which incorporates the Vericord S3 verification and system.

For further information contact: Philips Medical Systems, Kelvin House, 63–75 Glenthorne Road, Hammersmith, London W6 OLJ Tel: 081 741 1666

Quiz team win microwave oven

More than 130 people recently took part in the first Siemens' Medical Quiz, organized by the staff of the Manchester office. 26 teams from hospitals throughout the greater Manchester area participated, answering over 100 medical and general knowledge questions.

A team representing the Christie Hospital won the trophy and collected first prize — a Siemens microwave oven. Paul Hunter, Siemens' regional manager commented "the event proved to be very successful and generated a lot of enthusiasm among staff and participants alike — already people have been asking when the next quiz will be. Perhaps it will become an annual event."

Paul Hunter, regional manager Siemens Medical Engineering, Manchester presents the Siemens Medical Quiz trophy and first prize to captain of the winning team Richard Hopwell, District Superintendent.

100th Acuson 128XP for Hexham

Mr David James (R), Managing Director of Acuson UK, presents Dr Bruce Douglas with the 100th Acuson 128XP system.

For further information please contact: Acuson UK, Wiltron House, Rutherford Close, Stevenage, Herts.

QCT Bone Densitometry

New Automated Software for Improved Precision

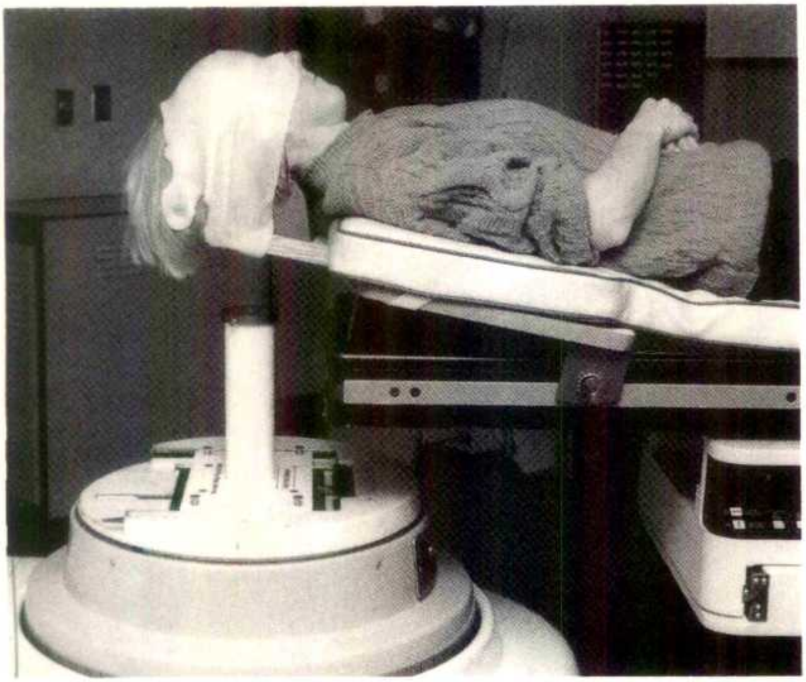
A new bone mineral analysis system from Image Analysis utilizes a solid calibration phantom and new automated software for improved performance and precision.

This is a highly sensitive method of measuring bone density using CT scanners — since these are widely available the QCT technique is a low cost way to quickly provide this diagnostic service.

During the 12 minute examination, the patient lies on the phantom while three CT slices are taken. The automated software provides a graphical output for comparison to normal bone density values. The QCT technique is reported to have the highest diagnostic accuracy for differentiating osteoporotics from normals.

For further information contact: Susan Cernik, Image Analysis, 17935-F Skypark Circle, Irvine CA 92714, USA (714) 250 7410

External Beam Stereotactic Radiotherapy From Northwest Medical Physics



A procedure for treating intracranial lesions has been developed which can be performed either with a single dose or in a course of fractionated radiotherapy. This system demonstrates distinct advantages over other systems and allows plenty of time for treatment planning.

The system utilizes three points as reference for the target location. Unlike head frames requiring a concentrated effort following rigid guidelines, this system relieves the user of this time pressure. Three gold markers provide a precise patient reference system allowing treatment to be repeated with equal precision at each fraction. A further advantage arises in the retreatment of adjacent lesions since prior radiotherapy can be accurately localized. These distinct clinical advantages are achieved with no compromise to the precision of the treatment.

For further information contact Northwest Medical Physics Center, 21031 67th Avenue West, Lynnwood WA 98036, USA. Fax: (206) 672 8470

Europe's longest modality link-up

3M have solved the imaging requirements of the newly opened £13 million west ward block of Singleton Hospital, Swansea. Fibre optic cables were used to image the maternity unit and one other ultrasound unit some distance apart from the main X-ray department. These link the modalities up to 1 mile away from the 3M Laser Imager System to increase imaging capacity and greater economical productivity. The present 2-year-old 3M Laser Imager System was upgraded by adding a 3M 1633 Multi-Modality Unit, and laying two 1000 ft fibre optic links. If the ultrasonographers need to query a scan in the Maternity Unit, they can telephone the radiologist in the main X-ray department where the images are produced, without having to leave the department. With the high image quality, reliability and versatility of the 3M Laser Imager System, there is the facility for further imaging devices to be added at a later date.

For further information contact Chris Varian, Medical Imaging Systems Group, 3M United Kingdom plc, 3M House, PO Box 1, Bracknell, Berkshire RG12 1JU. Tel: (0344) 858458.

BIR Calendar

Unless otherwise indicated, enquiries should be addressed to the Conference Manager, British Institute of Radiology, 36 Portland Place, London W1N 4AT (Tel. 071-436 7807).

Hypoxic cell sensitizers: do they have a future?
November 15, 1991
Organizer: Dr R. Camplejohn

Ischaemic heart disease — limitations of non-invasive assessment
November 22, 1991
Royal London Hospital
Organizer: Dr N. Garvie

Personal monitoring in the EC. Results and their implications
December 2, 1991
Organizer: Mr C. K. Bomford

Vascular systems imaging
January 24, 1992
Organizer: Dr J. F. Reidy

Radiosensitivity
February 11, 1992
Organizer: Dr M. Saunders

Quality standards in nuclear medicine
February 18, 1992
Organizer: Dr A. Smith

3-D image analysis in medical imaging
February 25, 1992
Organizer: Professor M. A. Smith

Megavoltage portal imaging
April 9, 1992
Joint meeting with IPSM
Organizer: Dr W. Jones

Radiology & Oncology '92
18–20 May 1992
International Convention Centre, Birmingham

The BIR Library is open weekdays 9 a.m.–5 p.m. (7 p.m. on Tuesdays and Thursdays).

The journal stock includes more than 100 titles. Though journals may not be taken out of the library, there is a photocopy service, also available by post or FAX. A list of current journals is available on request. Most books (excepting the historical collection) are available on loan.

Radiology & Oncology '92

Birmingham, 18 – 20 May 1992

The advance programme leaflet for Radiology & Oncology '92 has been circulated to members. Being the BIR's 50th Annual Congress the programme has been designed to satisfy the maximum range of members' interests. In the tradition of the BIR Congress, a good proportion of the review lectures will be from outside the UK with the US and Europe having a strong representation as in previous years.

The congress scientific programme committee welcomes proffered work. Please do study the subject areas as outlined in the programme leaflet and proffer work either as a paper or a poster. This year, Rad Magazine have generously offered to give a prize for the best poster in participating topic areas in recognition of the increasingly high quality of posters given at the Congress in recent years.

The Congress also offers a varied and exciting social programme including a concert and buffet supper at Symphony Hall which is being generously supported by Schering Health Care Ltd; an evening visit to the Patrick Car Colletction and the traditional BIR Annual Dinner. A Civic Reception and Pre-Congress Reception have also been arranged at no additional cost to registered delegates.

Should you have any queries on the Conference programme and social events or require additional copies of the registration form for distribution to colleagues do please contact myself, Elizabeth Carruthers and Charlotte McLeish in the conference office at 36 Portland Place.

We look forward to seeing you in Birmingham!

VANESSA WHITEHEAD
Conference Manager

SCOTTISH RADIOLOGICAL SOCIETY

The Annual General Meeting and Autumn Scientific Meeting of the Scottish Radiological Society will be held on Saturday 9th November 1991, 10.00 a.m. at:

Post-Graduate Centre
5 Lancaster Crescent
Glasgow

This will be followed at 2.00 p.m. by the **McGibbon Lecture** entitled

A day in the life of a London Radiologist

presented by Dr R. Dick of the Royal Free Hospital, London.

For further information please contact: Dr F. Calder, Victoria Infirmary, Glasgow.

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- INVITE YOUR COLLEAGUES TO JOIN YOU FOR COFFEE IN THE MEMBERS' ROOM

BIR Company Subscriber Scheme

The BIR company subscriber scheme is aimed at all companies with an interest in radiology and allied sciences.

For an annual subscription of £275 p.a. member companies are offered an attractive benefits package. To find out why your company should join the leading edge companies listed below, please contact Mr Tony Hudson, Administration Manager, British Institute of Radiology, 36 Portland Place, London W1N 4AT. Tel: 071-580 4085.

AEA Technology
Wigshaw Lane, Culcheth
WA3 4NE. Tel. 0925-252000 Ext. 4206
Product areas 7, 8.
Contact Mr J. G. Tyror, Director of Safety.

Agfa-Gevaert Ltd
27 Great West Road, Brentford, Middlesex
TW8 9AX. Tel. 081-560 2131.
Product Areas 1.
Contact Miss Anne Sparrow.

American Medical Ltd
PO Box 971, London SW10.
Tel. 071-352 8051. Fax: 071-376 4508.
Product areas 1, 3, 4, 5, 7, 8.
Contact Betsy Riley, Managing Director.

Amersham International PLC
Lincoln Place, Green End, Aylesbury,
Bucks HP20 2TP. Tel. 0296 395222.
Product areas 4, 5, 6.
Contact Mr C. M. T. Medley, Sales and Marketing Manager.

Bard Ltd
Forest House, Brighton Road, Crawley,
West Sussex RH11 9BP.
Tel. 0293 527888, ext. 2204.
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Room 525, Hinton House, Risley, Warrington, Cheshire WA3 6AS.
Tel. 0925 835022.
Product areas 8, 11.
Contact Dr R. J. Berry, Director of Health and Safety and Environmental Protection.

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HA3 6BZ. Tel. 081-954 2366.
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Contatct Mr D. Lewis, Sales Manager.

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33 Shallbourne Rise, Camberley GU1J
2EJ. Tel. 0276 64490.
Product areas: 1, 4, 5.
Contact Mr P. Supple, Managing Director of International Operations.

Cardiac Services Ltd
95A Finaghy Road, South Belfast
BT10 OBY. Tel. 0232-625566.
Product areas 1, 3, 4, 5, 6.
Contact Mr R. J. Brown. Managing Director.

Cea (UK) Ltd
25 Presley Way, Crownhill,
Milton Keynes MK8 0ES
Tel. 0908 263090. Fax: 0908 263546.
Product areas 1, 3, 4, 5, 6.
Contact John Dunster, Managing Director.

Clinical Press Ltd
Redland Green Farm, Redland, Bristol BS8
7HF. Tel. 0272 420526.
Product area 17.
Contact Dr Paul Goddard, Chairman.

Computer General
5 Greenway Business Park, Bellinger
Close, Chippenham, Wiltshire SN15 1BN.
Tel. 0249 445566. Fax. 0249 445595.
Product areas 1, 10.
Contact Alan Mawdsely, Division Manager/Yvonne Morris, Marketing Manager

Data-Med Computer Services Ltd
10 Faraday Building, Highfields Science
Park, University Boulevard, Nottingham
NG7 2QP.
Tel. 0602 431431. Fax: 0602 430782.
Product area 13.
Contact Mr C. Fildes, Sales Manager.

Du Pont (UK) Ltd
Wedgwood Way, Stevenage, Hertfordshire SG1 4QN.
Tel. 0438 734000.
Product areas 1, 3, 4, 5, 6, 7, 9 and 10.
Contact Mr E. G. Lovat, Product Manager, Diagnostic Imaging.

E. G. & G. Limited
Vale Road, Windsor, Berkshire SL4 5JP.
Tel. 0753 855611.
Product areas 1, 6, 7, 8.
Contact Mr Roy Hauton, Sales Executive (Therapy).

Elscint (GB) Ltd
Colonial Business Park, Colonial Way,
Watford, Herts WD2 4PT. Tel. 0923 39511.
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Contact Faith Gorman, Marketing Manager.

E-Z-EM Ltd
1230 High Road, Whetstone, London N20.
Tel. 081-446 9714.
Product areas 1, 2, 8.
Contact Richard Bayliss, Sales and Marketing Manager.

Fuji Photo Film (UK) Ltd
125 Finchley Road, London
NW3 6JH. Tel. 071-586 9351.
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Contact Mr R. G. Brown, Marketing and Administration Manager.

Gammex-RMI Ltd
34 Shakespeare Street, Nottingham
NG1 4FQ. Tel. 0602 483807.
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Contact Mr Brian Scott, Commercial Manager.

IGE Medical Systems Ltd
352 Buckingham Avenue, Slough, Berks
SL1 4ER. Tel. 0753 874000.
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PO Box 66, Station Road, Hemel
Hempstead, Herts HP1 1JU.
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Contact Mr J. J. G. Tweed, Manager, Health Sciences Division.

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HP9 2LR. Tel. 0494 791615/670586.
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3M House, Bracknell, PO Box 1,
Berks RG12 1JU. Tel. 0344 858000.
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Contact Mr Alan Budge, Marketing Manager.

Mallinckrodt Diagnostica (UK) Ltd
11 North Portway Close, Round Spinney,
Northampton NN3 4RQ. Tel. 0604-646132.
Product areas 4, 5.
Contact Mr D. G. L. Wood, Business Manager.

M. A. S. Medical Ltd
Armytage Road, Brighouse, West Yorkshire HD6 1QF. Tel. 0484 721906.
Contact Martin York, Managing Director.

Meadox (UK) Ltd
Matthew House, Matthew Street, Dunstable LU6 1SD. Tel. 0582 605111.
Product area 2.
Contact Mrs Sheila Heap, Sales and Marketing Manager.

Medical Xray Supplies Ltd
Unit 12, Kingsbury Industrial Estate, Church Lane, Kingsbury, London NW9 8AU. Tel. 081-205 9500.
Product area 1.
Contact Mr R. J. Laird, Sales Director/Mr K. Wartnaby, Managing Director.

Mitsubishi Electric UK Ltd
Travellers Lane, Hatfield, Herts AL10 8XB. Tel. 07072 78756.
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100 Voice Road, Carle Place, New York 11514-1593, USA. Tel. 516-741 7614.
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Contact Mr L. Birch Hansen, Managing Director.

Oxford Magnet Technology
Wharf Road, Eynsham, Oxford.
Tel. 0865 880880.
Product area 1.
Contact Pauline Hobday, Director of Sales and Marketing.

Philips Medical Systems
Kelvin House, 63–75 Glenthorne Road, Hammersmith, London W6 OLJ.
Tel. 081-741 1666.
Product areas 1, 2, 3, 4, 6, 9.
Contact Mr R. Van der Ploeg, Marketing Manager.

Premise Engineering Ltd
Tibbs Hill Road, Abbots Langley, Watford, Herts WD5 ODR.
Tel. 0923-267433/263320.
Product area 8.
Contact Mr R. K. Beach, Director.

Quantel Ltd
Administration Centre, Kiln Road, Newbury, Berkshire RG13 2HA.
Tel. 0444 232323.
Product areas 2, 10.
Contact Mr Christopher Trim, Publicity Officer.

Radiological Protection Services Ltd
61 Lind Road, Sutton, Surrey SM1 4PP.
Tel. 081-643 6374.
Product area 8.
Contact B. H. Cutting, Managing Director.

Schering Health Care Ltd
The Brow, Burgess Hill, West Sussex RH15 9NE. Tel. 0444 232323.
Product areas 1, 2, 3.
Contact Mr Simon Higginbotham or Mr S. Hearne, Product Managers.

Siemens plc
Siemens House, Windmill Road, Sunbury on Thames, Middlesex. Tel. 0932 752334.
Product areas: 1, 2, 3, 4, 6, 8, 9, 10, 13, 14, 15.
Contact L. J. McFadyen, Marketing Assistant.

Smith & Nephew Pharmaceuticals Ltd
Bampton Road, Harold Hill, Romford, RM3 8SL.
Product area 1.
Contact Mrs Annette Drake, Sales Manager

Sony (UK) Ltd
Jays Close, Viables, Basingstoke, Hants RG22 4SB. Tel. 0256 483564.
Product area 14.
Contact Richard Holt, Marketing Manager.

Toshiba Medical Systems UK
Manor Court, Manor Royal, Crawley, West Sussex RH10 2PY. Tel. 0293 560772.
Product areas 1, 2, 3, 4, 9, 10.
Contact Mr S. M. Weeden, Manager X-ray Products.

Toshiba Medical Systems Europe BV
Schieweg 1, 2627 An Delft, The Netherlands. Tel. 015 61 0121.
Product areas 1, 2, 3, 4, 9, 10.
Contact Mr P Blonk, Office Manager, X-ray BU.

Vertec Scientific Ltd
5 Comet House, Calleva Park Estate, Aldermaston, Reading RG7 4QW.
Contact Mr Frans Verlaan, Managing Director

Wardray Products Ltd
Hampton Court Estate, Summer Road, Thames Ditton, Surrey KT7 OSP.
Tel. 081-398 9911.
Product area 8.
Contact Mr R. B. Wardley, Managing Director.

William Cook (Eur) Ltd
6 Such Close, Letchworth, Hertfordshire SG6 1JF. Tel. 0462 482884 Fax: 0462 480944.
Product area 2.
Contact Tessa Phizacklea, Product Manager.

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8 Moody Street, Congleton, Cheshire CW12 4AP. Tel. 0260 279988.
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Contact Mrs P. Dhanani, Medical Sales.

KEY TO PRODUCT/ SERVICE AREAS

1: Diagnostic X-ray including NMR and CT
2: Interventional radiology
3: Ultrasound
4: Nuclear medicine
5: Radiopharmaceuticals
6: Radiotherapy and oncology
7: Radiobiology
8: Radiation protection
9: PACS
10: Image processing
11: Nuclear fuel cycle services
12: Quality assurance.
13. Radiology data management computer systems
14. Video printing
15. Equipment leasing
16. Hospital-shared services
17. Medical Publishing

Meetings and Courses

As a service to our readers, notices of meetings or courses will be inserted free of charge. Please send full details to the Honorary Editor, BIR Bulletin.

Thoracic Imaging Update
November 14, 1991
London
Further details: Margaret Johnson, National Heart & Lung Institute, London Chest Hospital, Bonner Road, London E2 9JX. Tel: 081-983 2342. Fax: 081-983 2202.

New Drugs for Asthma
November 14–15, 1991
London
Further details: Georgina Mason, IBC Technical Services Ltd, Bath House, 56 Holborn Viaduct, London EC1A 2EX. Tel: 071-236 4080. Fax: 071-489 0849.

6th Bristol Cardiac Ultrasound Course
November 18–21, 1991
Bristol
Further details: Dr Duncan Ettles, Dept. of Radiodiagnosis, Bristol Royal Infirmary, Marlborough Street, Bristol BS2 8HW. Tel: 0272-739746.

ROSAT-An X-ray Telescope in Space
November 20, 1991
Middlesex
Further details: John Sephton, National Physical Laboratory, Queens Road, Teddington, Middlesex TW11 OLW. Tel: 081-977 3222.

The Alan Nichols Memorial Lecture 1991
November 21, 1991
Oxford
Further details: Mr A.N. McNeill, Principal (Diagnostic), Oxford Regional School of Radiography. Tel: 0865 221748.

Implication of the new ICRP recommendations on radiological protection practices.
November 26–29, 1991
Salamanca, Spain
Further details: Commission of the European Communities, DG X11/D3, Rue de la Loi 200, B-1049, Brussels.

The Skeletal Survey in Non-Accidental Injury
November 28, 1991
London
Further details: Carol Curran, The College of Radiographers, 14 Upper Wimpole Street, London, W1M 8BN. Tel: 071-935 5726. Fax: 071-487 3483.

Improving Patient Care: The Biomedical Engineering Challenge
November 28, 1991
London
Further details: Christa Langan, The Fellowship of Engineering, 2 Little Smith Street, London SW1P 3DL. Tel: 071-222 2688.

15th Nottingham International Multi-Disciplinary Course on Breast Cancer Screening
December 2–4, 1991
Nottingham
Further details: Mrs B Price, Training Coordinator, Nottingham Breast Screening Training Centre, City Hospital, Hucknall Road, Nottingham NG5 1PB. Tel: 0602-691689. Fax: 0602-627707.

2nd International Congress on Oral Cancer
December 2–5, 1991
New Delhi, India
Further details: Sloane Hospital Travel Service, 204 Upper Richmond Road, London SW15 6TP. Tel: 081-785 2929. Fax: 081-788 8112.

The 3rd International Conference on Drug Delivery and Targeting Systems — Prospects for the 90's
December 5–6, 1991
London
Further details: Georgina Mason, IBC Technical Services Ltd, Bath House, (3rd Floor), 56 Holborn Viaduct, London EC1A 2EX. Tel: 071-236 4080. Fax: 071-489 0849.

Clinical Waste Incineration
December 10, 1991
London
Further details: Amanda Wright, IBC Technical Services, Bath House (3rd Floor), 56 Holborn Viaduct, London EC1A 2EX. Tel: 071-637 4383. Fax: 071-631 3214.

BMUS 23rd Annual Scientific Meeting and Ultrasound Equipment Exhibition
December 10–12, 1991
Bournemouth
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High Energy Photon Imaging at the Royal Marsden Hospital
December 11, 1991
Middlesex
Further details: John Sephton, Radiation Science Colloquia Organiser, National Physical Laboratory, Queens Road, Teddington, Middlesex TW11 OLW. Tel: 081-977 3222.

Advances in Heart Disease in Older People
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12th Annual Study Day, The Role of the Plain Abdominal Radiograph in the Acute Abdomen
December 13, 1991
Kent
Further details: Postgraduate Administrator, Kent Postgraduate Medical Centre, Kent & Canterbury Hospital, Canterbury, Kent CT1 3NG. Tel: (0227) 766887 Ext. 4361.

6th Asian Oceanian Congress of Radiology
December 14–18, 1991
New Delhi, India
Further details: M. L. Malhotra, Executive Secretary, Aggarwal Imaging Research Centre, 10-B, Kasturba Gandhi Marg, New Delhi-110 001, India.

Magnetic Resonance Basics at the University of Cambridge
December 15–20, 1991
Cambridge
Further details:Prof L D Hall, Herchel Smith Laboratory, University Forvie Site, Robinson Way, Cambridge CB2 2PZ. Fax: 0223-336748.

Mammographically Detected Early Breast Cancer
January 6–9, 1992
Naples, Florida
Further information: Dawne Ryals, Ryals and Associates, P.O. Box 1925, Roswell, Georgia 30077-1925, USA. Tel: (404) 641 9773. Fax: (404) 552 9859.

17th L.H. Gray Conference: Tumour assessment and response to therapy studied by MRS
April 13–16, 1992
University of Kent
Further details: Dr Marion Stubbs, CRC Biomedical Magnetic Resonance Research Group, Division of Biochemistry,
St. George's Hospital Medical School, Cranmer Terrace, London SW17 ORE. Tel: 081-672 9944 Ext 55809. Fax: 081-672 4864.

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Assurance of Quality in the Diagnostic X-Ray Department

The report of the BIR Diagnostic Methods Committee

Editors

J A Garrett, Director of Medical Equipment Management Organisation, Bristol & Weston Heath Authority, UK
D Gifford, Deputy Chief Physicist, Frenchay & Southmead Health Authorities, UK
M J Harvey, Middlesex Hospital, London, UK
P Goddard, Consultant Radiologist, Bristol Royal Infirmary, UK

Producing images, whether photographically or in electronic form, is the primary purpose of the diagnostic radiology department.

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The second section of the book presents the wider systems approach to quality assurance with reference to recent standards for QA and how these may be applied to diagnostic radiology.

The final part discusses quality assurance in computer assisted imaging, computed tomography, magnetic resonance imaging, and digital subtraction angiography.

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OPTIMIZATION OF IMAGE QUALITY AND PATIENT EXPOSURE IN DIAGNOSTIC RADIOLOGY
(BIR Report 20)

Editors:
B M Moores, B F Wall, H Eriskat and H Schibilla.

Contents: Introduction. Image Perception. Physical Assessment of Image Quality. Clinical Assessment of Image Quality. Optimization of Image Quality and Patient Dose - Paediatric Radiology - Mammography - Chest Radiography - Technical Factors. Patient Dose Measurements and Quality Assurance. CEC Image Quality and Exposure Criteria Trial. Panel Discussions. Conclusions and Perspectives for Future Research. CEC Study Group Document on Quality Criteria for Diagnostic Radiographic Images.

Key components in quality assurance in diagnostic radiology are image quality and patient exposure. Quality criteria defining optimum procedures should ensure that the most accurate and reproducible diagnostic information is obtained from radiographs, but at the same time minimize exposure of the patient to ionizing radiation. Formulation of such criteria was the aim of a workshop organized jointly by the CEC and NRPB, of which this book is the edited proceedings. A revised list of quality criteria for common diagnostic examinations was drawn up by a CEC Study Group and is appended to the proceedings.

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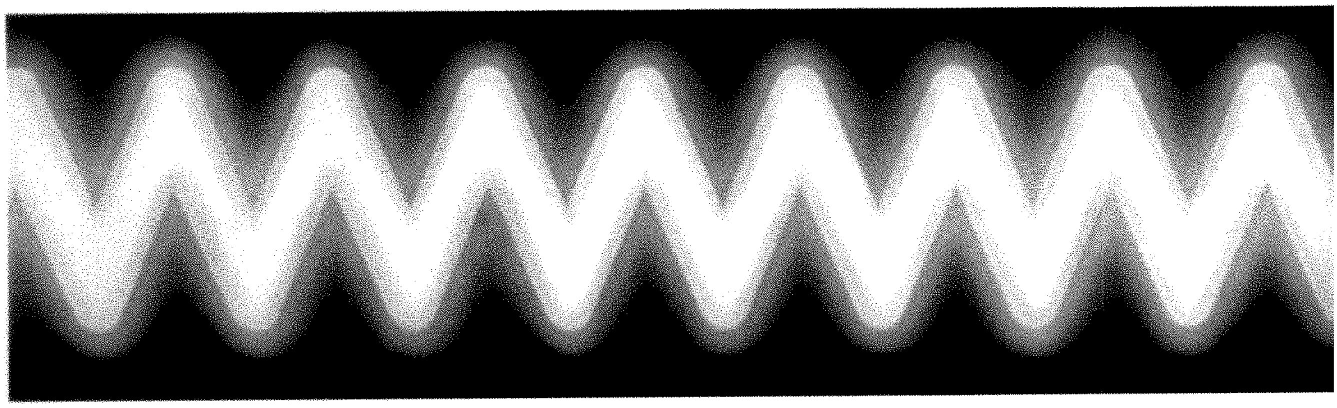

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(BIR Report 19)

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N J McNally, Gray Laboratory, Mount Vernon Hospital, Middlesex

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There are excellent reviews on modern theories of fractionation and of the new clinical options in dose fractionation. The growing significance of vascular approaches to treating cancer is reported in papers on the vasculature of tumours, the activation of bioreductive drugs, and the manipulation of blood flow for therapeutic benefit. Chemical modifiers, both sensitisers and protection, are discussed at both the experimental and the clinical level. The important and growing subject of prognostic indicators is reviewed with papers on prediction of radiosensitivity, repopulation and the possible role of PET scanning for functional measurements. Finally, two papers review the current status of the clinical use of hyperthermia.

These proceedings will be of interest to all who are concerned with the treatment of cancer by radiation, and provide an excellent basis for anyone who wishes to undertake research in experimental radiotherapy.

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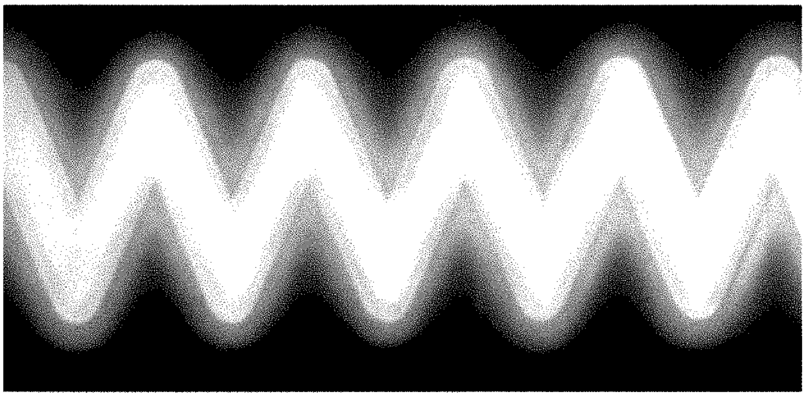

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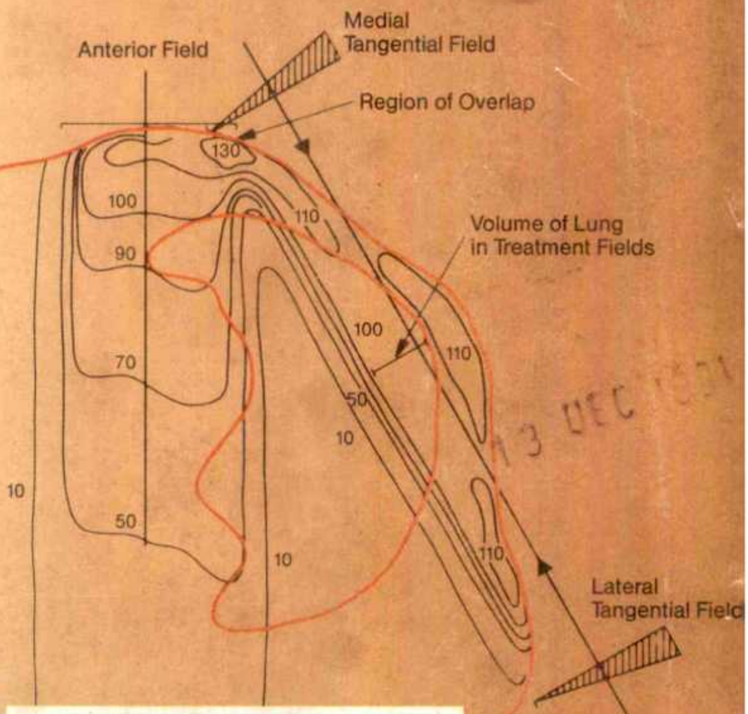

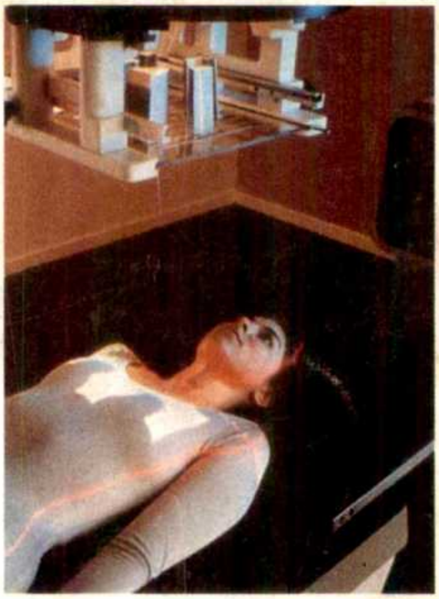

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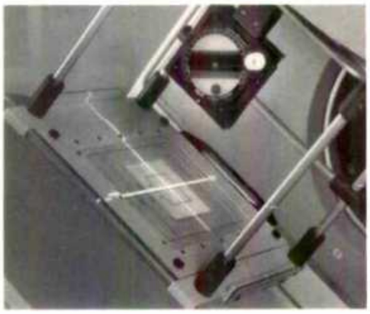

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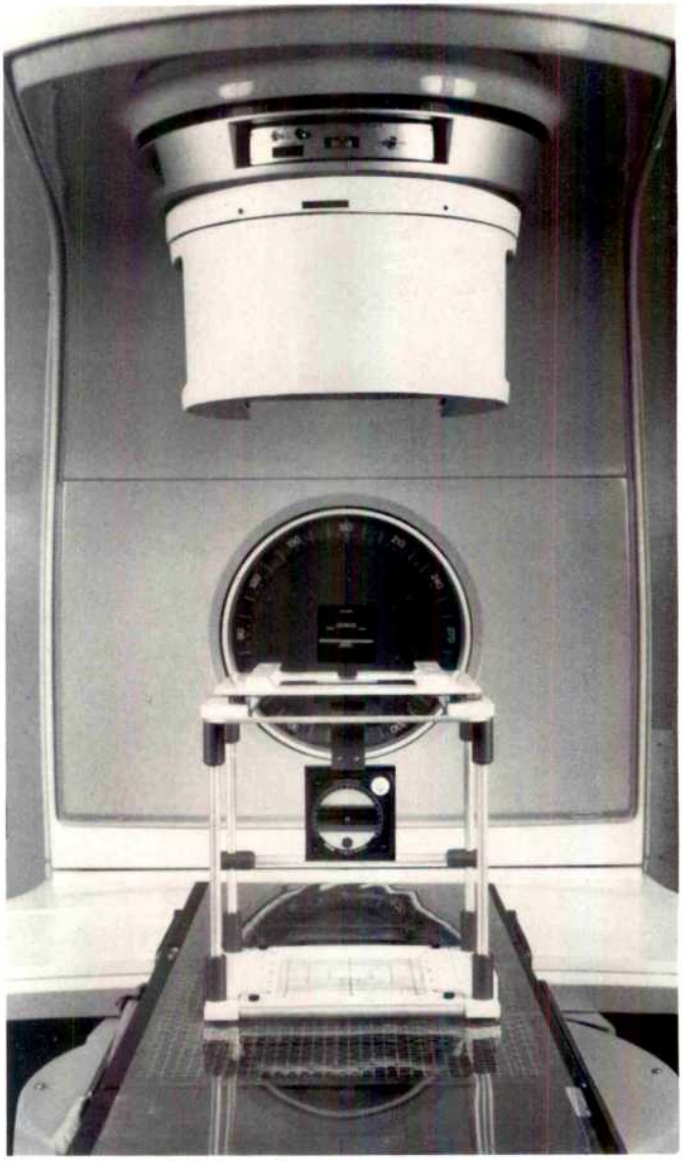

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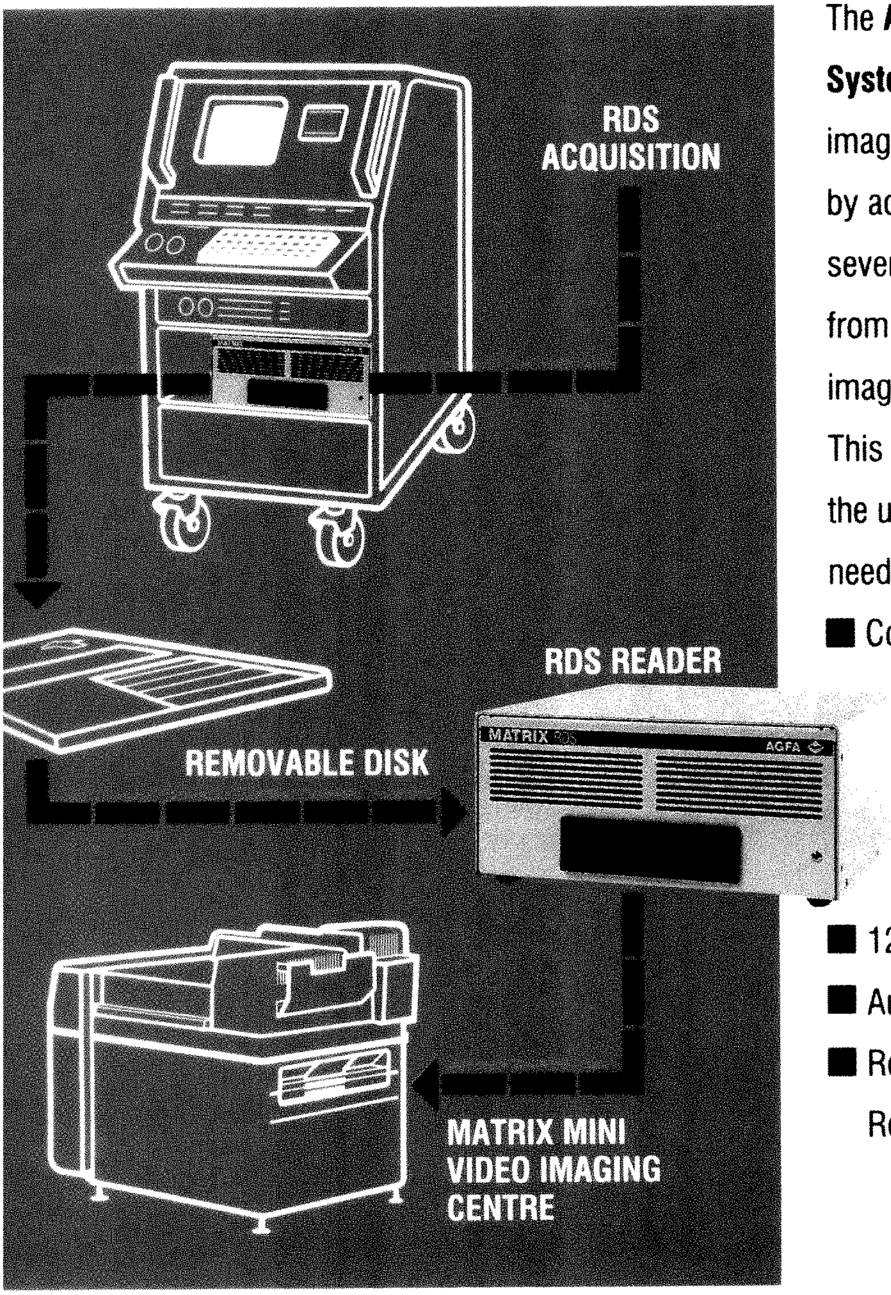

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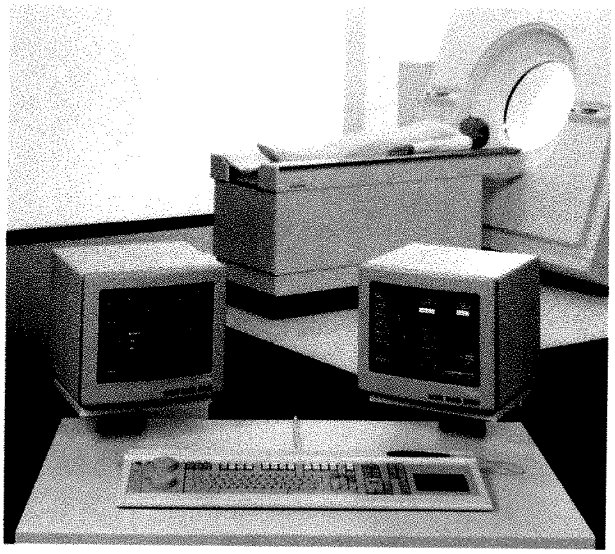

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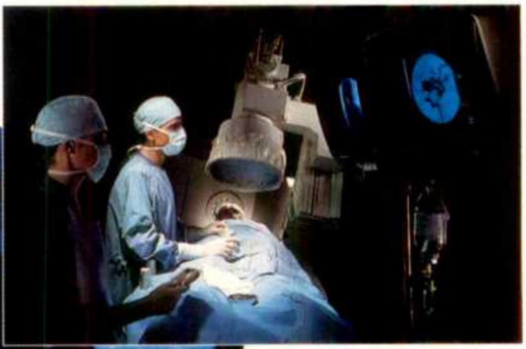

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Review article

Advances in basic science: have they benefited patients with cancer?*

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(*Received May 1991*)

Keywords: Basic science, Cancer treatment, Radiobiology, Radiotherapy

Sir James McKenzie Davidson was a practising ophthalmic surgeon at the time of the report of Röntgen's discovery of X rays in December 1895. He was quick to perceive the potential application in medicine; within weeks he had built his own apparatus and by February 1896 was producing X-ray pictures, including one of the foot with six digits, which was published in a new journal *The Archives of Skiagraphy*. By the summer of 1897 he had visited Röntgen in Germany and moved to London in order to devote himself to radiology and was engaged in demonstrating its value widely in medicine. He did, for example, in that year, draw attention to the importance of X rays to the diagnosis of urinary calculi, publishing a radiograph of a bladder stone (Burrows, 1986).

McKenzie Davidson, a true pioneer in the application of radiology to medicine, through the two decades in which he worked prior to his untimely death in 1919, stressed the fundamental importance of a knowledge of physics and he himself was actively engaged applying it to radiology right up to the time of his death.

In the past 70 years radiology has expanded beyond the imagination of anyone, even the like of McKenzie Davidson. Diagnostic imaging has been divided into a number of separate disciplines and the therapeutic application has long since separated to become clinical oncology.

In the training required to pursue any aspect of radiology or clinical oncology, stress is laid on the fundamental sciences and this surely is something of which McKenzie Davidson would have approved. For the Fellowship in Clinical Oncology there is a Part I examination and the candidates are tested on their knowledge of pathology, physics, radiobiology and medical statistics.

The candidates have, I know, a mixed attitude to the subject that they must study, keenness and enthusiasm to pursue their chosen field being tempered with some scepticism as to the value of these fundamental sciences. This is sometimes confirmed when established consultants in the field sympathize with their registrars and talk of necessary hurdles rather than important and relevant subjects to master.

This questioning has some foundation, for if we look at those areas in oncology where there appears to have been the greatest clinical advance in recent years—children's tumours, lymphomas, testicular tumours—the most important ingredient has been careful clinical observation, and although the randomized controlled clinical trial has been important in securing some advances, in others this has been achieved by simple retrospective comparison of results achieved in sequentially treated groups of patients (Birch et al, 1988; Peckham, 1988; Coiffier et al, 1991; Murphy & Magrath, 1991; Rosenburg, 1991). It has been the clinical programming of chemotherapy, rather than the discovery of new agents, that has given benefit and the radiotherapy employed has been that based on a long routine practice.

Scepticism of the value of the fundamental sciences and their products is sometimes shared by the general public and those who must fund the medical services. Although there may be the excitement of new advances, there is also talk of expensive doctors' toys satisfying their personal ambitions and fascination for technology, and of debilitating side-effects.

I should like to look at the contributions of the basic sciences and attempt to measure the benefit that the cancer patient may have derived in recent years.

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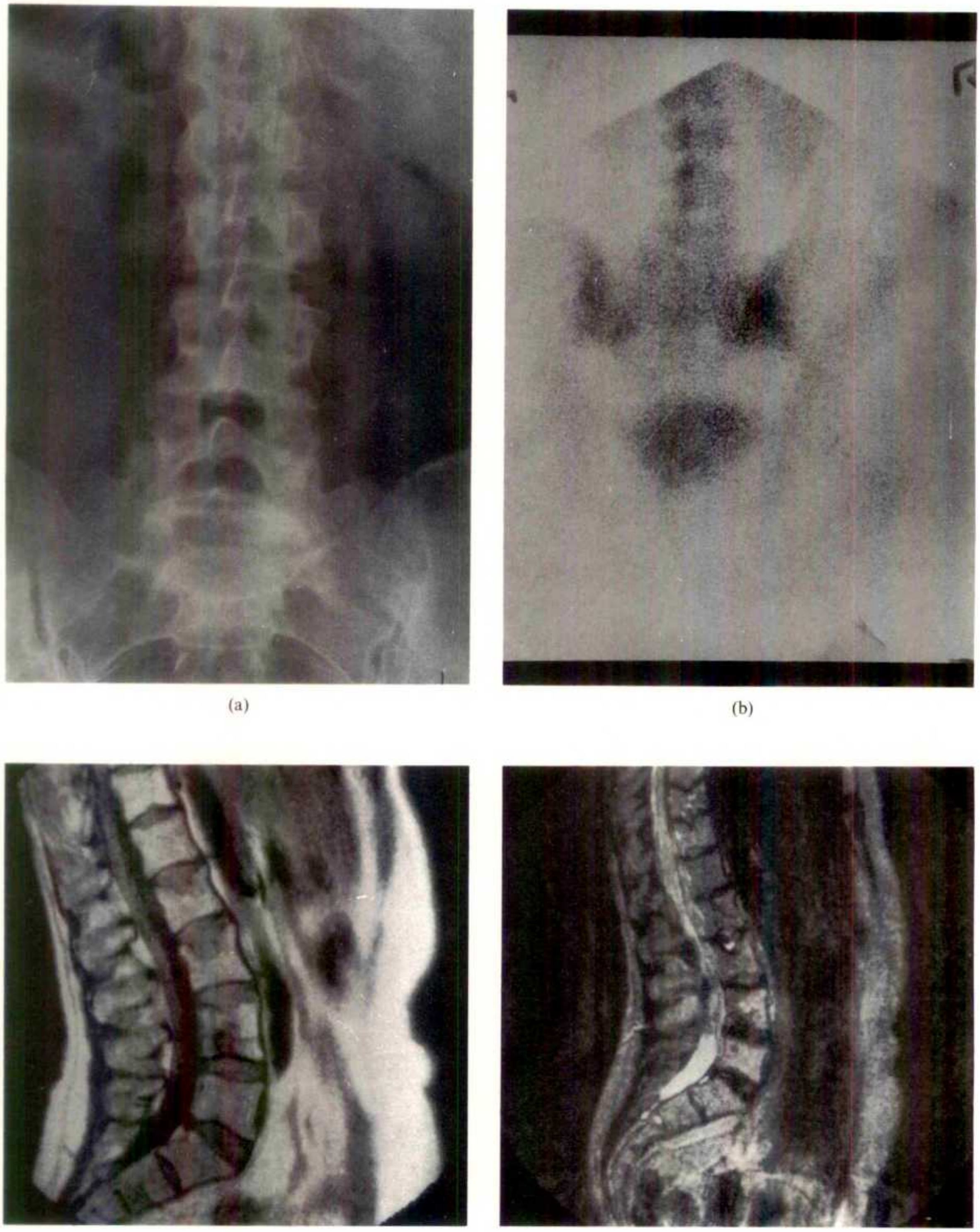
*Mackenzie Davidson Memorial Lecture presented at Radiology and Oncology Conference, Brighton, 29 April–1 May 1991.



(a) (b)

(c) (d)

Figure 1. A patient with known carcinoma of breast complained of severe low back pain. Radiographs of the lumbar spine (a) and of the pelvis showed no definite evidence for metastases and a bone scan (b) similarly gave no evidence for their presence. An MRI scan (c) showed metastasis in the body of the fourth lumbar vertebra and (d) tumour in the spinal canal from the level of L1 to L5.

It is certainly appropriate to start with diagnosis and the determination of the extent of tumour, and, here, as a result of great endeavours in physics and engineering, we have all the new imaging that our diagnostic colleagues can now provide. There have been great advances in conventional radiology and the developments in isotope scanning, ultrasound, positron emission tomography (PET), computed tomography (CT) and magnetic resonance imaging (MRI). We see in our day-to-day practice the improved imaging of tumours that has resulted. At Mount Vernon we are fortunate to have a Scanning Centre within our Cancer Treatment Centre, with Hiram Baddeley and Wabi Ayoub as our radiologists.

We can now so much more effectively assess tumours at presentation in order to find their true extent, locally and distant, in order to plan the best management. We can find numerous examples of the value of CT in the management of tumours of the head, neck and chest, and the contribution of MRI scanning to the management of tumours of the spinal cord and brain has been outstanding (Fig. 1).

It is, of course, not enough to demonstrate the value in an individual case. We must look at large groups and determine whether, overall, a clear advantage is shown. In our own work we have shown the superiority of CT over conventional radiography in the imaging of bronchial carcinoma before treatment and feel that it is now mandatory to perform CT if one is to select the right patients for radical treatment (Table I) (Lyn et al, 1991a).

The transfer of CT images to treatment planning computers has enabled us to improve greatly the precision and reproducibility of treatment plans for radiotherapy. Automatic correction can be made, without intensive labour and error, for the inhomogeneities in density that alter the dose distribution through the tissues irradiated. The way is open for multislice imaging and planning in three dimensions and the possibility of conformation therapy.

Table I. A series of 93 patients with carcinoma of the bronchus considered for radical radiotherapy. The results of X-ray and CT examinations were compared. Sixteen areas of spread from the primary tumour were seen in both studies but 82 areas of extension were revealed only by CT (Lyn et al, 1991a)

Spread to	Seen on both CXR and CT	Only on CXR	Only on CT
Hilar nodes	7	—	13
Mediastinal nodes	5	—	26
Pleura over tumour	4	—	31
Diaphragm	—	—	1
Chest wall	—	—	4
Effusion	—	—	6
Lung wide of primary	—	—	1
	16	0	82

CXR = chest X ray.

The response of tumours to treatment can be most clearly seen and here again in lung cancer we have shown the superiority of CT over conventional radiography of the chest (Table II) (Lyn et al, 1991b). The diagnosis of distant metastases, which may be aided by the new imaging techniques, is not only important in deciding the right management for the patient at presentation, but also in gaining relief of symptoms. Particularly in the correct management of metastasis to the spine, our radiologists have given us outstanding service using MRI.

The case for the great advantage to the patient of all the new imaging techniques seems overwhelming; however, there are problems. In our enthusiasm with shades of grey we can overinterpret a result and this can lead to wrong management. Where resources are limited, as here in the UK, there is the expense of the investigation. Would the money be better spent on other aspects of patient care? Is the use of expensive imaging techniques in the diagnosis of a recurrence of tumour justified when the procedure itself may add to the discomfort of the patient, when there may be only limited possibilities of treatment and the chance of long-term survival does not exist?

Considerable efforts have been made to make overall assessments of new imaging techniques. Moore & Dixon (1987) performed a cost–benefit analysis of the introduction of a CT scanner at Cambridge and suggested that their scanner had re-paid three times its cost (Table III). There will, of course, be great differences in the cost–benefit ratio when we compare this situation where there is just a single body scanner for 1 million people, with strict criteria for use, with other situations. The pressure of case referral and its pattern, the quality of the radiographers and the radiologists, the type of scanner available, the alternative apparatus for investigation, local enthusiasm and prejudice all have their influences.

Table II. The response to radical radiotherapy was assessed in 58 patients. No residual tumour was seen on the chest X ray in 25 cases, but only in 11 could this be confidently reported as other changes obscured the area of interest in 14. With CT, 20 of 22 studies could be confidently reported as showing no tumour (Lyn et al, 1991b)

	No tumour seen		Residual tumour	
	CXR	CT	CXR	CT
Satisfactory studies	11	20	33	36
Unsatisfactory—obscuration by collapse fibrosis, etc.	14	2	—	—

CXR = chest X ray.

Table III. A cost–benefit analysis for the year 1983/84 performed by Moore & Dixon (1987), concerning a CT scanner installed at Cambridge. There was considerable saving because alternative investigations, including surgical procedures and other radiological investigations, were not required. A cost–benefit ratio of 1 : 3.07 was obtained

	£
Cost	
Radiologist	27,000
Radiographers and other staff	34,000
Consumables	56,000
Electricity, heating, etc.	6,000
Capital cost	58,000
Building cost	2,000
Maintenance contract	35,000
Total	218,000
Benefit	
Inpatient days saved	364,000
Outpatients visits saved	19,000
Tests saved	290,000
Total	673,000

The concepts of sensitivity (true positivity) and specificity (true negativity) can be applied, but in every situation such concepts have to be tested against alternative methods of diagnosis and finally against the clinical value of the findings achieved. Statistical analysis may be helpful and it is here that another of the disciplines that the trainee in clinical oncology must master may be important. However, we face a formidable task in the ultimate assessment: "Is the diagnostic technique of value in relation to outcome?" Can knowledge gained in diagnosis lead to a measurable improvement in patient survival or in quality of life? I doubt if the true overall value of a hospital-based CT scanner can be measured by any statistical method. The collection of accurate data can only be performed by limiting the spectrum of disease examined and in so doing this greatly limits the value of the assessment; there are just too many inter-related variables. In the long run it will be the clinical judgement of the physician and the wide experience of the radiologist, tempered by effective review in specific situations and sharpened by economic considerations, that will best resolve this question.

Advances in physics and engineering, together with computer technology, have brought us a new generation of treatment machines. It is a long way from the old 250 kV apparatus that was manhandled by our radiographers (introduced 60 years ago and now only finally being phased out of our British radiotherapy centres) to the new high-energy apparatus. These machines, weighing several tons, rotate so that the central ray of the beam does not deviate from a circle only a millimetre in diameter. There have been great advances in the accuracy of dosimetry and in quality assurance. Verification systems double-check on the setting of the machine for each treatment. We know of unfortunate disasters that have led to much patient suffering because of errors in the dose delivered, and so are pleased to employ machines with such safety features.

We have to recognize, however, that the introduction of such machines, with their extreme sensitivity to the most minor deviation to ensure safety, does alter work practices. Whereas at times of pressure our old linear accelerators at Mount Vernon (11 and 18 years in service) can treat over 60 patients in a long working day we can, at best, treat 36 on our newest and most magnificent machine. The implications of costing the workload of a busy centre are, therefore, considerable. Through the whole of medicine, improved standards of safety have most considerable cost implications—an important fact commonly overlooked by those who agitate for such standards.

Particularly in the last decade, we have seen an explosion of knowledge in molecular biology. We have all struggled to become conversant with a whole new vocabulary—oncogenes, tumour suppressor genes, antioncogenes, antisense oligonucleotides and many, many others. Sometimes every paper within a general journal such as the *Lancet* describes some new knowledge gained using a technique within the field of molecular biology. In cancer a vast amount of fundamental knowledge has been gained concerned with DNA and the processes by which growth is controlled (Renan, 1990). There are exciting possibilities for intervention at the nuclear level to modify genes to prevent cancer or to modify the course once it has developed (Hochhauser & Harris, 1991). We may learn the process of development of resistance to cytotoxic drugs and how to modify it. These are possibilities that will require many years of development and certainly we cannot expect them before the turn of the century. Recalling McKenzie Davidson, we cannot but make the contrast between Röntgen's discovery of X rays and their application in medicine within weeks; however, the discoveries are so different.

The use of monoclonal antibodies tagged with radioisotopes is leading to new diagnostic techniques and their value in certain situations in oncology is now being established. Therapeutic applications are in an earlier stage of development (Goldenburg, 1991).

It is in our longest established basic science, pathology, that the monoclonal antibodies have had their greatest impact in routine practice. Our colleagues in histopathology would be lost now without them. The anaplastic tumour of unknown site and type of origin is now uncommon, for appropriate monoclonal antibodies can reveal markers indicating the tissue of origin. There can be little doubt that in clinical practice the refinements in histological diagnosis influence the management of many cases. Extension of the use of monoclonal antibodies in pathology gives the opportunity to determine many factors that may be of prognostic importance.

Radiobiology, of all the basic sciences, is most fundamental to radiotherapy. We in Britain can take great pride in the major contributions that have been made from this country and in the high standing of British radiobiological science throughout the world. The oxygen effect must certainly be given our first consideration. Mottram, working at Mount Vernon in the 1930s, clearly established the picture now familiar to all radiotherapists (Mottram, 1935). Not only was oxygen important to radiosensitivity, but there was good evidence that human tumours were often hypoxic. The work was carried on by Gray and his colleagues (Gray et al, 1953), who brought it to wide attention, and by many other workers in this country and overseas, working both in the laboratory and in the clinic, where over 70 randomized controlled trials have been performed. Hyperbaric oxygen and the chemical sensitizing agents have been the approaches most studied (Dische, 1989). The basic science of medical statistics allowed the full analysis of this material. After examining the results we must conclude that no technique has shown, in any tumour, a consistent margin of benefit to justify routine use. We must acknowledge that so far we have failed to advance the care of the cancer patient. What are the lessons to be learnt from this experience and has the effort been entirely wasted? (Dische, 1991a).

Firstly, there can be no doubt that during conventional fractionated radiotherapy, reoxygenation occurs and is highly effective in dealing with hypoxic cells in many human tumours. There is, however, evidence that in some tumours, at some sites, hypoxia does remain a cause for failure and that methods to sensitize hypoxic cells may be of benefit (Dische, 1991a). The identification of this minority of patients is essential before a method to sensitize hypoxic cells can be shown to be of value. Probes for the identification of hypoxic cells are being developed (Hodgkiss et al, 1991), but we need to know not just the proportion of hypoxic cells before initiation of therapy, but also the sequence of changes that occur in that fraction during therapy.

Secondly, we have learnt that we must take into consideration all the factors that influence the radiosensitivity of the tumour and not just merely pursue one of them. It is quite probable that a tumour which shows a cell kinetic pattern with a capacity for rapid proliferation is also one which, as a consequence of that rapidity of proliferation, shows a high degree of hypoxia. To use an hypoxic cell sensitizer with a conventional protracted scheme of radiotherapy over 5–7 weeks must, in such a case, lead to failure, as repopulation during the intervals between treatments will easily make up for all the extra cell kill achieved in the hypoxic cells (Dische, 1991b).

Thirdly, not only is there a complexity in the factors that influence tumour response, but any method employed may have more than one effect. As an example, many of the nitroimidazoles are vasoactive and a redistribution of blood supply caused by them may negate any benefit achieved with hypoxic cell sensitization (Murray et al, 1987; Chaplin, personal communication). Furthermore, effects at different dosage levels may be markedly different in animals and in man. We need only to know the situation in the patient using the clinically relevant dosage.

Fourthly, it is evident that the translation from the laboratory model to the patient with a malignant tumour involves a tremendous leap. There is a need to match the precision of laboratory science with clinical science, which observes with precision human physiology and the responses of normal tissues, as well as tumour, to radiation.

Despite the failure so far we have, in the pursuit of hypoxia, learnt a good deal about tumours and clinical trials. The practice of determining tumour concentration in patients given drugs was pioneered with the chemical sensitizing agents (Gray et al, 1976; Workman, 1989) and is now being used in the study of cytotoxic drugs; however, the hypoxic tumour cell remains very resistant to radiation and undoubtedly is the cause of failure to cure in some cases. Techniques are being developed to identify hypoxic cells in the clinic (Chapman et al, 1989; Hodgkiss et al, 1991). Recent evidence from the laboratory suggests that the most effective method of raising the oxygen tension in tumour is by a relatively simple technique of breathing oxygen with 5% carbon dioxide at atmospheric pressure in combination with nicotinamide, which prevents transient hypoxia owing to spasm of small vessels (Rojas, 1991; Rojas, personal communication). As an extension of the work with hypoxia, the combination of agents to increase tumour hypoxia temporarily with agents that concentrate in hypoxic cells to which they are cytotoxic is being explored (Chapman et al, 1989). Clinical benefit may yet be gained from all the knowledge concerned with the oxygen effect.

One of the most exciting recent developments in tumour biology has been the study of the cell kinetics of human tumours and the influence it has had on the dose fractionation of clinical radiotherapy. In the past, cell kinetics could only be determined by the administration of tritiated thymidine, which gave a considerable burden of radiation exposure. Only patients with very advanced disease could be the subjects of such a study and, furthermore, the technique was a laborious one requiring many weeks for a result to be obtained. Now with the administration of a small dose of bromodeoxyuridine (BrdUrD) and the sampling of the tumour 4–6 h later, it is possible with analysis using a cell sorter, to obtain cell kinetic data within 24 h of biopsy. This technique, introduced and developed by Adrian Begg, Nic McNally and George Wilson at the Gray Laboratory, has revolutionized our knowledge (Begg et al, 1985; Wilson et al, 1988; Dische et al, 1989).

At Mount Vernon we have now studied over 400 human tumours. The labelling index and the duration of S phase have been determined and from these the potential cell doubling time (T_{pot}) has been calculated (Fig. 2) (Denekamp, 1982). There is a wide range of values for tumours at each of the sites, but in our largest group, the head and neck patients with squamous tumours, the mean potential cell doubling time is less than 5 days. This can be contrasted with the volume doubling time

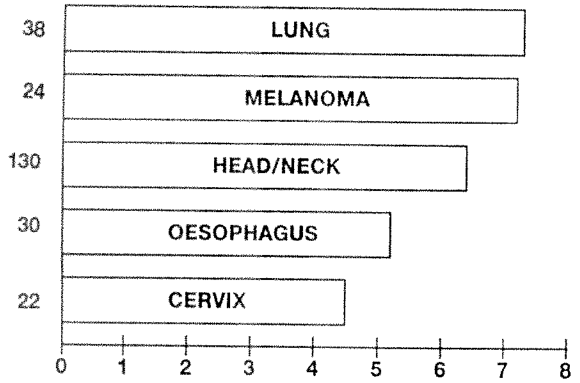


Figure 2. Median T_{pot} (days) of 244 human tumours according to site.

commonly seen in human tumours, which ranges from 30 to 90 days (Steel & Lamerton, 1966; Denekamp, 1982). Because of these relatively long times, radiotherapists have not in the past been concerned that tumours may in fact grow during a conventional course of radiotherapy. The reason why there is such a big difference between the potential cell doubling time and the actual volume doubling time is that most cells produced do not proceed to further cell division but degenerate or differentiate, and, in some cases, enter a resting phase. When, as after the first few doses in a conventional course of radiotherapy, the number of surviving cells is markedly reduced, the situation is greatly changed and the full potential for rapid cellular production is likely to be realized. The histological study of the uptake of BrdUrD has shown that the T_{pot} in some human tumours may be as short as 1–2 days (Dische et al, 1989).

The obvious way to get over this capacity for repopulation is to shorten the overall duration of the course of radiotherapy as much as we can. Unfortunately, if large doses are given in daily treatments in a short period of time, to achieve a satisfactory tumour dose the acute and late radiation damage to normal tissue is extremely severe.

Fortunately, alongside the evidence about the kinetics of human tumours have appeared data to suggest that giving treatment in many small doses does lead to a reduction of late damage (Barendsen, 1982; Fowler, 1988). It is, of course, late damage appearing more than 6 months after conclusion of the course that is the main constraint on total dose in conventional radiotherapy. The linear-quadratic equation has greatly advanced our understanding in this area. Cellular damage is inflicted by an α component of radiation that is linearly associated with dose, and by a β component that is related quadratically (Barendsen, 1982; Fowler, 1988). At clinically relevant doses, the α element dominates in tumour and acutely responding tissues such as the mucosa and the skin, but in the vascular and connective tissues, which are most important with regard to late effects, the β element becomes more important. It follows that if radiation doses are given in small increments there is considerably less damage in the late-responding tissues.

In order to combine the shortening of overall treatment time to overcome the problem of repopulation, and to minimize damage in the late-responding tissues, we need to give treatment on more than one occasion on each treatment day.

During the last 20 years, as this evidence slowly accumulated, many clinical experiments have been performed in fractionation. Out of the vast mass of data some important patterns are now apparent, which will irrevocably alter clinical radiotherapy for the future.

It has been found that giving the commonly used 2 Gy dose on three occasions each day in order to achieve a full tumour dose in a period of 2 working weeks leads to an unacceptable level of immediate and late morbidity (Peracchia & Salti, 1981). Many workers have given as much dosage as they can safely do in a period of 2 weeks or so and then have allowed a rest period of 3–4 weeks before finally concluding treatment with a boost dose (Van den Bogaert et al, 1982; Wang, 1988). Although some very good results have been reported in pilot studies (Van den Bogaert et al, 1982; Wang et al, 1986; Wang, 1988), a randomized controlled trial has not shown an advantage (Van den Bogaert et al, 1986). It seems likely that the rest period negated any benefit achieved in the first intensive phase, as any tumour cells surviving may have so proliferated that the final boost will have been inadequate to eliminate them. It is essential to reduce the overall period of treatment and in the current EORTC study, although a rest period is employed, the overall duration has been reduced from 7 to 5 weeks (Begg et al, 1990).

In Houston, Peters and his colleagues have pioneered the "concomitant boost" (Knee et al, 1985; Ang et al, 1990). The main course of radiotherapy is given to known tumour and the area of possible spread over a period of 6 weeks. The extra treatment given to the area of known tumour that would normally follow is, however, applied as a second treatment each day during the last 2 weeks of the main course. Only a full randomized study will show whether the results of standard conventional treatment will be bettered in this way.

In 1984, Michele Saunders and I, together with Jack Fowler and Julie Denekamp, performed a review of all the data available at that time. As a result we designed Continuous, Hyperfractionated, Accelerated Radiotherapy (CHART) (Saunders & Dische, 1986). There were to be no intervals once the therapy was begun, not even for the weekend, for obviously tumours did not recognize the sanctity of the weekend. As acute reactions would limit the amount of treatment that could be given, the whole course should be completed before any treatment reaction appeared. Knowing that when you accelerate treatment in the management of head and neck tumours marked mucosal reactions usually appear on the 13th or 14th day, we decided on a 12-day period. It was essential to give small dose increments and so we decided on a scheme in which 36 treatments, initially of 1.4 Gy and then of 1.5 Gy, were given three times a day for 12 days. A 6-h interval was allowed between treatment on each day in order to enable as much recovery as possible of sublethal injury (Saunders & Dische, 1986; Saunders et al, in press).

The first group of patients, three with carcinoma of the bronchus and one with an advanced tonsillar carcinoma, were treated in January 1985. Two of those original four patients are alive and well at over 6 years and we have now treated well over 300 patients. In our main treatment groups, the more advanced head and neck cancers and locally advanced carcinoma of bronchus, we have obtained results significantly better than those attained previously at our centre with conventional radiotherapy (Saunders et al, in press). As a result of this the Medical Research Council, the Cancer Research Campaign and the Department of Health have established a CHART Steering Committee under the Chairmanship of Professor Ann Barrett and randomized controlled trials are underway in head and neck and bronchial cancer. Although these trials only started at the beginning of April 1990, in a year we have gathered nearly 400 cases and are well pleased with progress. One of the most important features of the trial is a quality assurance programme to help maintain a high standard through all the centres involved—nine in the United Kingdom and two in continental Europe.

Although an improvement in local tumour control is the prime intention of both studies, we are now, with long-term follow up of the patients in our pilot study, seeing the second theoretical advantage—a reduction in late radiation change (Saunders et al, in press). We have seen regrowth of hair in skin fully irradiated and a complete recovery in the mucosa of the mouth so that the patients are able to preserve their remaining teeth in good condition or to wear dentures without difficulty. This is partly due to the fact that salivary function recovers to a much greater extent than after conventional radiotherapy (Leslie & Dische, in press). Our only setback in the area of post-radiation change has been an incidence of radiation myelitis and here it would seem that in the spinal cord there is an exceptionally long half-time of recovery of sub-lethal injury (Dische & Saunders, 1989; Dische, 1991c). An adjustment of permitted dose has been made for spinal cord and we hope that this particular problem has been overcome.

In oncology, with improved tumour control and prolonged survival of patients, the minimization of late normal-tissue injury becomes more and more important. Our patients wish not only to be cured, but to live out totally normal lives. CHART does give the promise of increased tumour control, combined with reduction in late tissue damage.

The integration of all methods to improve tumour control in radiotherapy has already been stressed. If accelerated treatment can increase tumour control and overcome the problem of repopulation, then there is further potential for improvement if methods to overcome resistance of hypoxic tumour cells can be added and if further tumour cell destruction can be achieved using cytotoxic drugs. A number of research groups are presently measuring the radiosensitivity of human tumours in the laboratory and relating their findings to the clinical result (Davidson et al, 1990; Peters, 1990). With knowledge of inherent radiosensitivity, hypoxia and cell kinetics, we have the possibility of precise biological planning of radiotherapy.

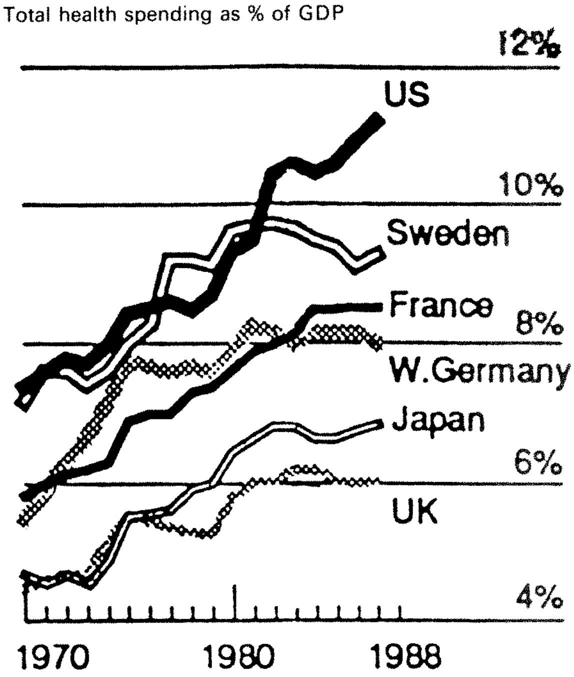


Figure 3. Total health spending as a percentage of gross domestic product in six countries over the period 1970–1988 (Organization for Economic Co-operation & Development, 1989).

We have been successful in obtaining funding for the randomized controlled clinical trials of CHART; this at a time when there have been so many problems because of inadequate financing of research. We are only too well aware that in our country we spend too little on health compared with other developed countries in Western Europe and in North America (Fig. 3). We have had to get used to the continual shrinkage of real amounts of money for science and you may not be aware that the Medical Research Council, in its desperate plight to manage on shrinking finances, has disproportionately reduced its expenditure on cancer research (Fig. 4); this at a time when deaths due to neoplasms as a percentage of all deaths have risen from 20.2% in 1970 to 25.1% in 1986 (Fig. 5). The cancer charities, the Cancer Research Campaign and the ICRF, together with others, have done their best to expand their fund-raising but it is sad to see a reduction in national spending on cancer research; this in a country where the standard of living of the large majority has risen over the years (HMSO, 1990). There seems more interest in expanding the holiday market than in expanding healthcare and research.

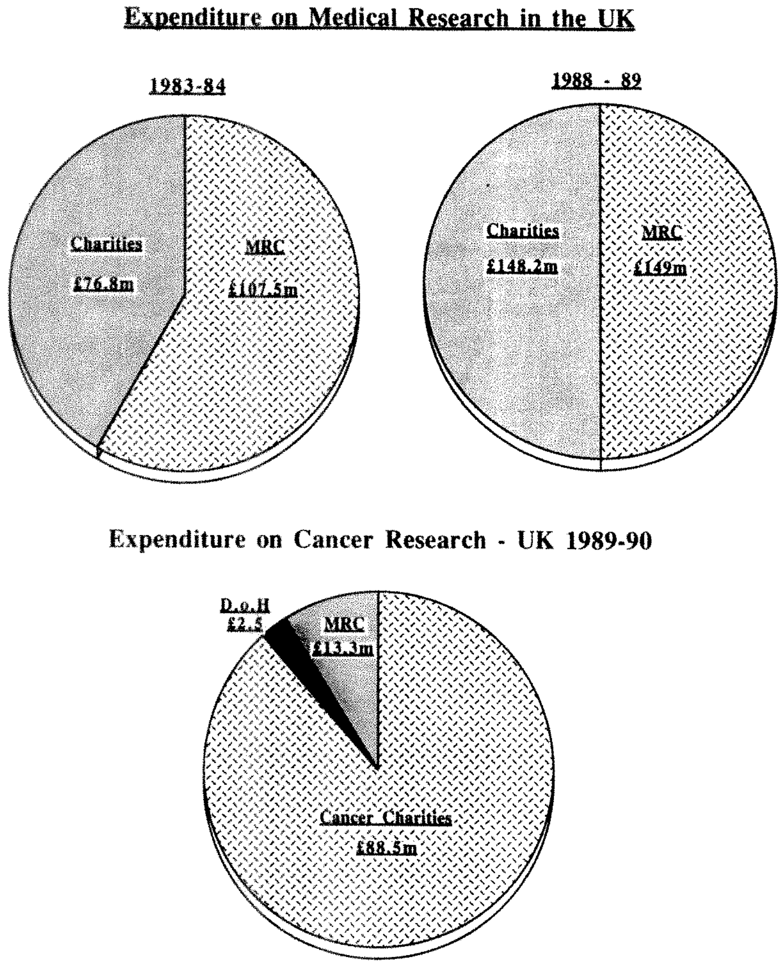


Figure 4. The changing proportion of medical research funded by the Medical Research Council and by the research charities over a 5-year period. In real terms the contribution of the Medical Research Council has fallen by approximately 3% per annum and that of the cancer charities has risen by 10% per annum. Only 15% of cancer research was Government funded in 1989–90. Research by the pharmaceutical industry is not included (Galloway, 1989).

Medical audit is now a popular word, stimulated by the Government's White Paper. The reform of the Health Service is going to be achieved with patient care set at a high standard by medical audit. It seems new and yet is not audit just one aspect of clinical research that has always set the standard for medical care? When a clinical trial is performed all aspects are considered and set to a high level in order that the measure being tested is the only one at variation through both trial groups.

Meanwhile, a vast amount of time is spent by some of our most able people in judging the work of their peers in order best to decide where the limited resources that are available should be spent. Even when the highest commendation is agreed, there is no security of funding and priority tends to be given to those areas having the highest profile and the greatest public interest, such as screening, molecular biology and AIDS; other good research may founder for lack of support.

We do recognize in this new world that we must compete for resources. Health must compete with education, defence and all the other areas of national expenditure and then, within health, oncology must compete with cardiology, nephrology, community care and all the other specialties. It is not enough that we are treating a serious, life-threatening condition; we must show that we give real benefit perhaps even in terms of quality-adjusted life years. Within oncology the various disciplines must show their merit, and advances in surgery, cytotoxic chemotherapy and radiotherapy may lead to a different balance in the use of such modalities in any one disease. We must co-operate and compete with our colleagues in other disciplines involved in cancer care. Advances will not come easily and will only occur where there is a proper provision and organization of resources for fundamental and for clinical research; furthermore, both must work together. In clinical radiotherapy that provision is most inadequate with academic posts decreasing rather than increasing in number in recent years. Clinicians must recognize their importance, help with the foundation of academic units and give them their support.

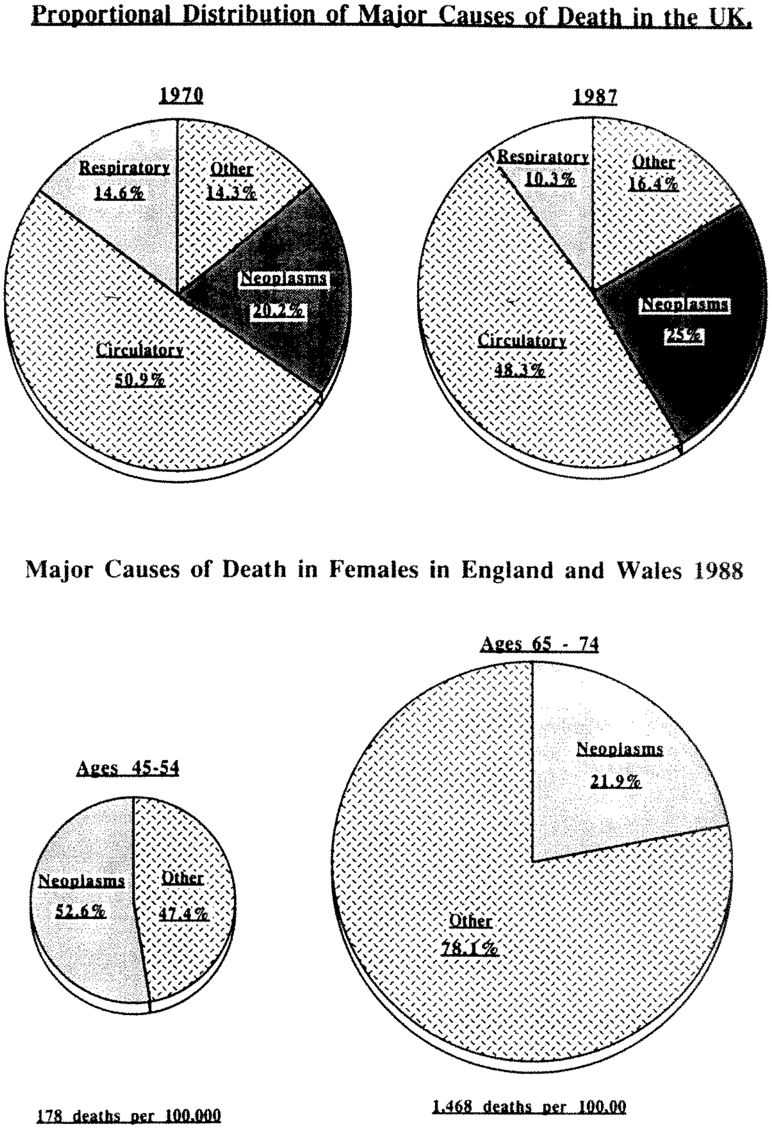


Figure 5. The proportional distribution of the main causes of death in the UK is compared with that for 1970. Neoplasm as a primary cause of death rose from 20.2% to 25.0% over this time (Office of Health Economics, 1989). The major causes of death in females aged 45–54 years are compared with those aged 65–74 years in England and Wales in 1988. Neoplasms account for more than half in the younger group compared with less than a quarter in the older women (Office of Health Economics, 1989).

In my title I have set the question "Has the cancer patient derived benefit from basic research?" The answer is certainly "yes". Only a proportion of all patients with cancer have been directly helped by research that has been discussed here, but the influence of this research has extended so that benefit has been given to all those who come to our centres for cancer treatment. This is because research sets high standards for care and attracts and stimulates the brightest minds to the problems of the cancer patient; it encourages patients and staff that current techniques which have only partial success are going to be improved and that the care will improve. Research adds to the interest and excitement of everyday work. We cannot, therefore, just take advantage of the advances achieved by our colleagues in North America and continental Europe, where greater resources are devoted to health and research, but we must ourselves actively pursue research at all levels from the laboratory bench to the bedside.

As in all branches of medicine, and as in all human activities, we must constantly renew our work otherwise standards of care will fall. It is in this that research is so important.

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Sonographic evaluation of the parotid ducts: its use in tumour localization

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Keywords: Parotid ducts, Sonography, Tumour localization

Abstract. The previously unreported sonographic anatomy of the intraglandular parotid ducts is described, and how this aids tumour localization is illustrated. Forty patients underwent ultrasonography and computed tomography (CT) sialography for the evaluation of parotid tumours. Ultrasound identified two extra unsuspected 5 mm tumours in the superficial lobe, which could not be seen at CT. Both techniques produced similar results for deep and mixed lobe lesions. Ultrasound had one false positive mixed lesion, which surgery subsequently found to be confined to the deep lobe. The full extent of invasion in three deep lobe tumours was revealed only by CT to be parotid invasion by nasopharyngeal carcinomas. We conclude that parotid sonography with reference to the intraglandular ducts is highly accurate in localizing parotid tumours and should probably be the first-line imaging technique. Computed tomography should only be necessary for visualization of deep lobe tumour extent and in those cases where the complete tumour boundary cannot be seen by ultrasound alone.

Identification of the course of the facial nerve through the parotid gland and hence division into deep and superficial lobes is of surgical relevance. Until recently, there has been no direct method that could image the facial nerve. Magnetic resonance imaging (MRI) identifies the main trunk and is arguably the best method for showing parotid tumour (Mandelblatt et al, 1987; Wortham et al, 1989). D'Alimonte et al (1989) found that MRI was much better than ultrasound at predicting facial nerve involvement. However, relatively few departments have this option and so we describe the sonography of the intraglandular ducts to enhance the accuracy of ultrasound tumour localization. Its use relies on the fact that tumours displace the ducts because of their mass effect. In our experience this is often different from inflammatory lesions that appear to spread around the ducts (Fig. 1). Smith et al (1987) showed that 82% of tumours on computed tomography (CT) sialography could be visualized well in relation to Stenson's duct with correct lobe differentiation.

We describe sonography of the parotid ducts and correlate the duct displacement patterns with CT sialography in parotid tumours.

Methods

Forty patients presenting with parotid masses underwent CT sialography and ultrasound. An Aloka 650 system with a linear 5 MHz probe and stand-off medium was used to image transversely and longitudinally through both glands and down the neck for lymph nodes. Stenson's duct was seen as two parallel white lines with an echo-poor central area in contradistinction to the intraglandular ducts, which were seen as short (2–4 mm), single, scattered white lines reflecting the arborizing duct pattern seen at sialography. We had observed these lines scattered through normal parotid glands and so to prove that these were indeed the intraglandular ducts, Stenson's duct was cannulated in volunteers as for a routine sialogram and air (2–3 ml) was injected. (Normal saline injection was used initially but was not conclusive and so air was used in preference to enhance the contrast.) Gas bubbles could be seen travelling along these white lines causing them to be ill defined and brighter, some producing "comet" tail artefact proving that these were ducts as previously thought (Fig. 2). Unfortunately, this is a painful procedure and could not be undertaken satisfactorily in patients, so it was only used to verify our duct theory.

All the patients had 5 mm contiguous slices through the parotid glands on a GE 8800 scanner and gantry tilt was used appropriately to avoid dental amalgum. Stenson's duct was cannulated and 1–2 ml of dilute (60%) meglumine iothalamate 280 mgI/ml was injected. The CT criterion for tumour localization was the relationship to Stenson's duct, the superficial lobe being lateral and the deep lobe medial to this (Smith et al, 1987). A mixed lobe tumour was diagnosed when it appeared to involve both lobes.

Similar criteria were used for sonography, but in addition the main direction of the intraglandular duct displacement by the tumour was noted. The relationship of the tumour bulk to the angle of the mandible was recorded (Whyte & Byrne, 1987). All the patients underwent surgical resection.

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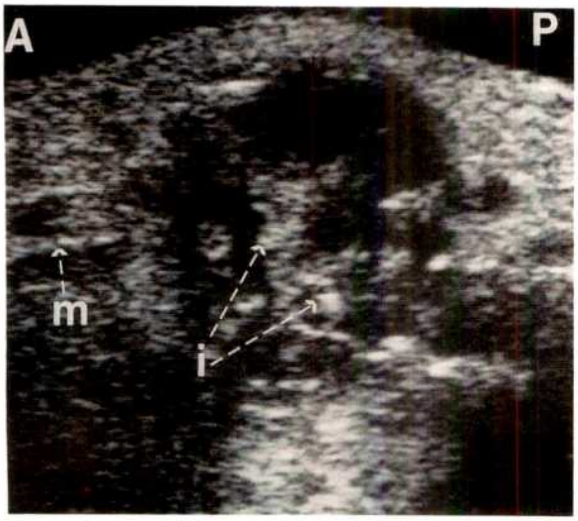


Figure 1. Transverse section through the parotid gland showing an ill defined inflammatory mass lesion invading around the ducts (i = intraglandular ducts, m = mandible).

Results

Surgery discovered 42 tumours in the 40 patients. The tumour diameter ranged from 0.5–6.0 cm (mean 2.4 cm), with 40% malignant on histology.

Ultrasound diagnosed all the 42 lesions, whereas CT missed two small tumours (< 5 mm) located in the superficial lobe. The results are summarized in Table I. This shows that CT accurately diagnosed all the mixed and deep tumours, whereas ultrasound diagnosed one false positive mixed tumour that restrospectively should have been labelled as deep, as some small peripheral ducts had been misinterpreted (Figs 3, 4).

Table I. Comparison of preoperative CT and ultrasound of 42 parotid tumours with surgical findings

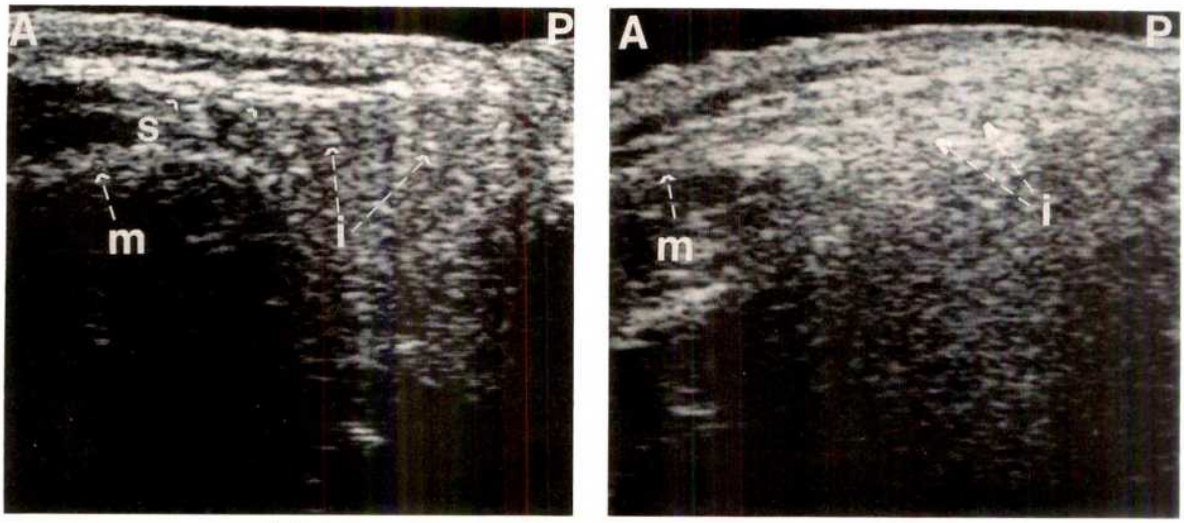
	Surgery	CT	Ultrasound
Superficial lobe	27	25	27
Mixed	8	8	9
Deep lobe	7	7	6
Total	42	40	42

Three of the deep lobe tumours correctly located by CT and ultrasound were due to nasopharyngeal carcinoma invading into the parotid gland, but ultrasound failed to show the full extent that CT clearly portrayed (Fig. 5).

All the patients had surgical resection of the tumour and surgical findings were then correlated with the imaging.

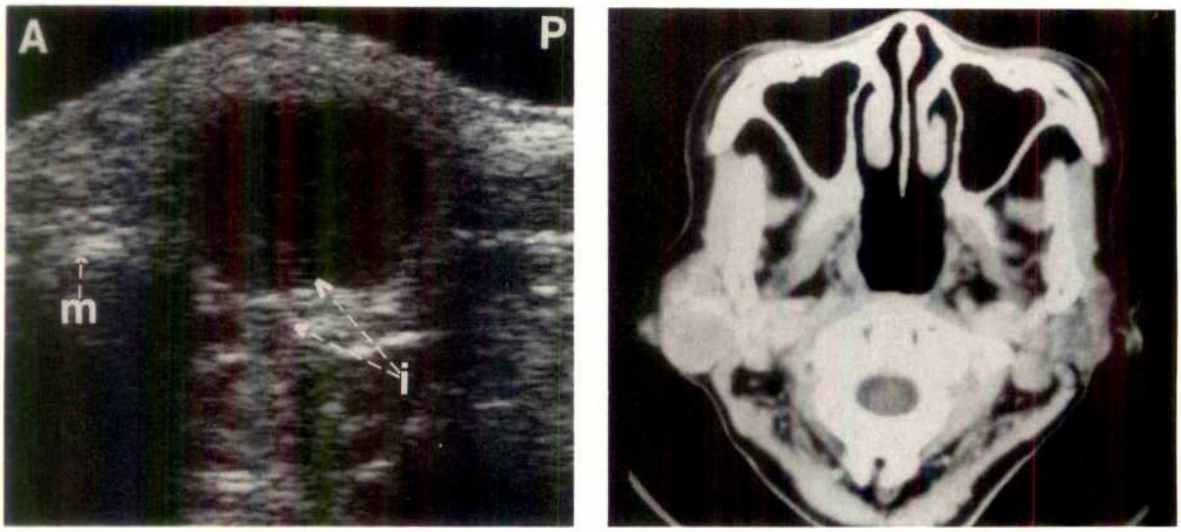
Discussion

Parotid sonography has been described in the diagnosis of many conditions including sialolithiasis, sialectasis and neoplastic and inflammatory disease (Wittich et al, 1985; Bruneton et al, 1987). Authors have strived for many years to locate accurately parotid tumours to define their extent and predict facial nerve involvement. Direct evidence of facial nerve compression or invasion by tumour has only relatively recently been described using MRI (Mandelblatt et al, 1987; D'Alimonte et al, 1989). Many indirect methods for tumour localization on CT and ultrasound have been described with less satisfactory results. These include the tumour relationship to the styloid process, external carotid artery, retro-



(a) (b)

Figure 2. (a) Transverse section through a normal parotid gland showing Stenson's and intraglandular ducts (s = Stenson's duct, i = intraglandular ducts, m = mandible). (b) The intraglandular ducts become brighter and ill defined after injection of 1–2 ml of air into Stenson's duct in this normal parotid gland (i = intraglandular ducts, m = mandible).

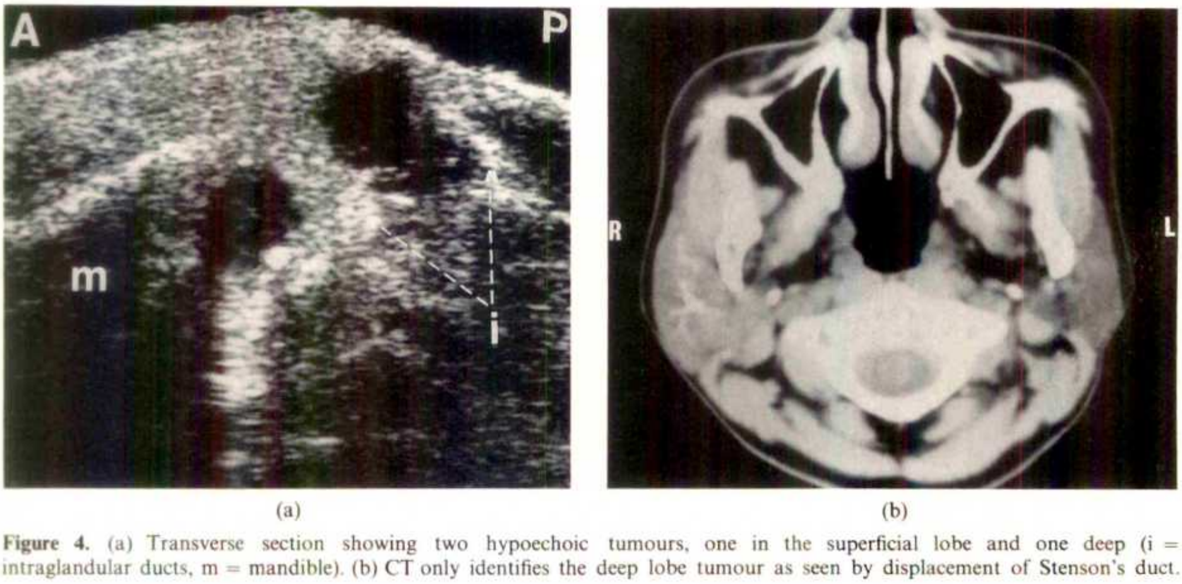


(a) (b)

Figure 3. Hypoechoic superficial lobe tumour compressing the ducts medially (m = mandible, i = intraglandular ducts). (b) CT sialography confirms a superficial lobe tumour in the same patient.

mandibular vein, Stenson's duct, posterior belly of diagastric or an 8.5 mm arc from the posterior mandibular ramus (Rice et al, 1980; Stone et al, 1981; Conn et al, 1983; Smith et al, 1987).

Sialography has relied on intraglandular duct displacement for tumour diagnosis and therefore if this duct detail is superimposed on the ultrasonogram then this should enhance its tumour localization accuracy. If the arborizing intraglandular duct anatomy is considered as seen on the sialogram, then this may explain our ultrasound description of these ducts. The normal parotid gland appears hypoechoic compared with the masseter muscle and consistently has short, scattered white lines throughout the gland. This ultrasound description fits with our concept of the arborizing duct nature, as only small sections of duct are seen in any one image. We presume that these ducts appear as single white lines and not tubular structures as in Stenson's duct, as they must be smaller than the resolution of the equipment. All the tumours in this series appeared hypoechoic compared with the adjacent gland parenchyma and it is known that many tumours may produce "through transmission" simulating a cystic lesion, especially if the tumour is strongly hypoechoic



(a) (b)

Figure 4. (a) Transverse section showing two hypoechoic tumours, one in the superficial lobe and one deep (i = intraglandular ducts, m = mandible). (b) CT only identifies the deep lobe tumour as seen by displacement of Stenson's duct.

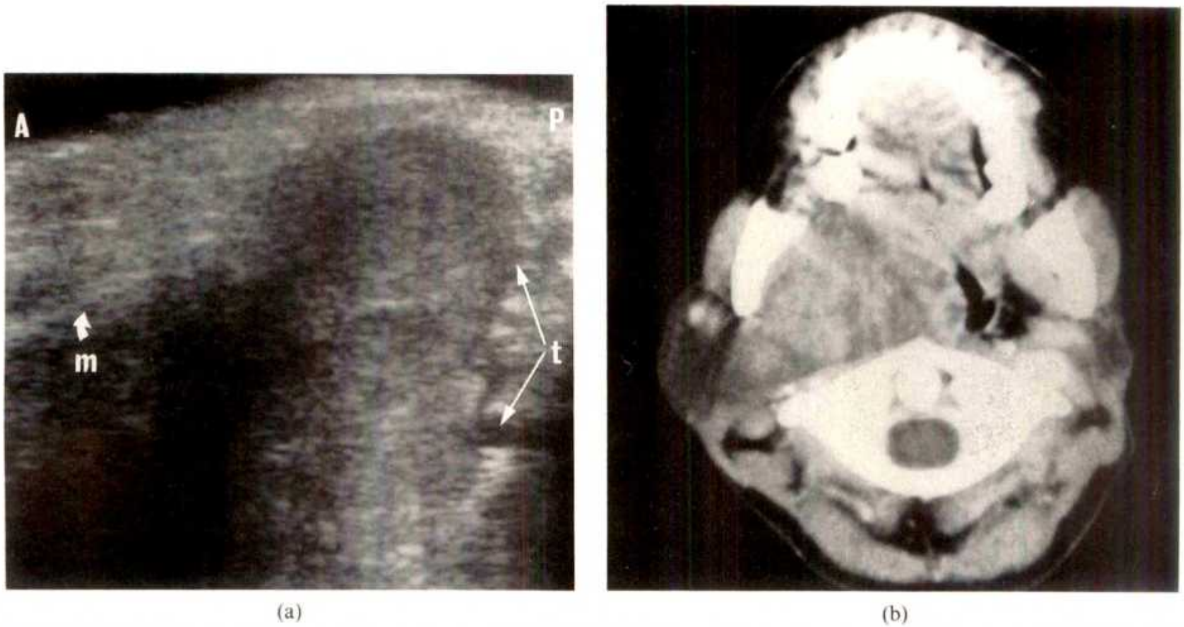


Figure 5. (a) Ultrasound cannot penetrate deep enough to see the full extent of this tumour (t = tumour, m = mandible). (b) CT shows the tumour to be a nasopharyngeal carcinoma invading the parotid gland.

(Bruneton et al, 1987). However, this sign should not be confused with duct displacement as the ducts may be seen as described, even in these areas of high reflectivity.

The sensitivity of high-resolution sonography in the identification of the parotid tumour approaches 100% (Wittich et al, 1985). In this study, ultrasound visualized 100% of the tumours showing greater sensitivity than CT. However, perhaps if 2 mm scans can be performed then this may enhance the CT sensitivity. However, CT may still lack the tumour/parenchyma contrast differentiation that makes the tumour so easily identifiable sonographically.

Parotid sonography is a non-invasive technique that can offer accurate information for tumour localization. Computed tomography is helpful for the deep lobe tumour extent and in those cases where ultrasound cannot define the full tumour boundary in a large lesion. Knowing that 80–90% of parotid tumours are in the superficial lobe, then parotid sonography should be all the imaging that is necessary in the majority of cases.

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The radiological (CT) and clinical sequelae of primary intracerebral haemorrhage

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Keywords: Intracerebral haemorrhage, Brain haemorrhage, Computed tomography, Stroke, Chinese

Abstract. To determine the radiological and clinical outcome of primary intracerebral haemorrhage, a prospective study was carried out involving computed tomography (CT) of 388 consecutive Chinese patients admitted with acute stroke to a large public hospital in Hong Kong. Further CT and functional assessment were performed 3 months later in 71% of survivors. The patients were admitted over a 6 month period. 120 (31%) were found to have had presumed primary intracerebral haemorrhage. Of these, 64 patients (53%) died within 3 months. From 40 of the 56 survivors who returned for a follow-up study at 3 months, 30 were functionally independent and five mildly disabled; only five were significantly disabled. Follow-up CT showed no residual lesion in 27%, low attenuation areas in 37%, slit-like lesions in 25% and calcification in 10% of patients. The size of residual lesions correlated statistically with the degree of residual disability, although the association was not close. It is concluded that primary intracerebral haemorrhage accounts for a high percentage of strokes among Hong Kong Chinese with more than half of the patients dying within 3 months. Many survivors, in whom follow-up CT appearances are variable, show good functional recovery.

Since the advent of computed tomography (CT), it has been possible to detect intraparenchymal brain haemorrhage with a high degree of sensitivity and specificity (Dolinskas et al, 1977; Sandercock et al, 1985; Adams & Victor, 1989). An intracerebral haematoma appears on CT as a homogeneous, well-defined area of hyperattenuation which may be surrounded by a zone of low attenuation attributable to oedema, ischaemia or clot retraction (Savoiardo, 1986). At some stage, which may be as early as 2 weeks (Dennis et al, 1987), the haematoma becomes isodense with the surrounding brain and later may leave a smaller area of low attenuation (Messina & Chernik, 1975). Occasional reports have documented complete resolution of the lesion to the extent that a follow-up CT would be considered normal (Helweg-Larsen et al, 1984). A porencephalic cavity described as "slit-like" (Dolinskas et al, 1977) or an area of calcification (Helweg-Larsen et al, 1984; Fieschi et al, 1988) has also been observed. However, the factors affecting the formation of such long term changes and their clinical significance have not been studied in a systematic, prospective manner.

We report the CT findings in 40 survivors of a consecutive series of patients with primary intracerebral haemorrhage (PICH). We included in our definition of PICH all cases of intraaxial brain haemorrhage which were apparently unrelated to trauma, tumour or haemorrhagic infarction. The acute and follow-up (at 3 months) scans were compared and correlated with the patient's degree of functional recovery.

Methods

Between January and June 1989, all patients admitted to the Prince of Wales Hospital with a diagnosis of acute stroke were studied. The Prince of Wales Hospital is a large public hospital in the Eastern New Territories of Hong Kong serving a population of approximately one million. Patients recruited to the study were examined by a neurologist within 24 h of admission and had CT of the brain within 1 week of ictus, and within 48 h in most cases.

Patients who survived the acute stroke were seen again after 3 months, when a functional assessment according to the Barthel Activities of Daily Living (ADL) Scale (Wade et al, 1985) and a repeat CT were performed.

CT was performed without contrast enhancement on a GE8800 scanner using 10 mm slices and interpreted by a single radiologist. The greatest diameter of each lesion was measured. For slit-like lesions the length was measured. "Calcifications" were areas of hyperattenuation on follow-up scans at the site of the original haematoma.

The Spearman correlation was used to determine whether the size of lesions seen on follow-up was related to the Barthel score.

Results

Over 6 months 388 patients with acute stroke, all of whom were Chinese, were admitted. 120 (31%) were identified by initial CT as having intracerebral haemorrhage, presumed to be primary. 64 (53%) of these died during the first 3 months and of the remaining 56 patients, 42 returned for follow-up at 3 months. Repeat CT of the brain was obtained on 40 of these patients, 27

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males and 13 females. The mean age for males was 67 years and for females 55 years. Three patients had a past history of stroke and 21 (53%) gave a history of hypertension. Of the 14 patients who did not return for follow-up, eight had moved away and six were unable to attend (*vide infra*).

Initial CT

Of the 40 survivors studied, the haematoma was in the putamen in 18, the thalamus in 12, the mid-brain and pons in five and in the cortex and subcortex in four cases. One patient who subsequently made a complete recovery had an intraventricular haemorrhage.

The haematomas were rounded, the largest being 7 × 4 cm and the smallest 0·8 × 0.8 cm.

Follow-up CT

On follow-up CT, 11 patients (27%) had complete resolution of the haematoma and four (10%) had a minimal area (less than 0.5 cm in diameter) of low attenuation. 11 (27%) had a larger, rounded residual area of low attenuation which measured up to 2.5 cm in diameter. In a further four patients (10%) there was significant calcification within the area of low attenuation. Slit-like or less commonly comma-shaped lesions (Fig. 1) were encountered in the follow-up CT of the remaining 10 patients (25%). The longest slit-like lesion measured 5.5 cm and the shortest 1 cm. Calcification was also evident in two of these slit-like lesions (Fig. 2).

In Table I, the appearances of the lesions seen on follow-up are related to the size of the original haematoma. In general, the smaller the haematoma the more likely it was to resolve completely. Larger haematomas tended to become either rounded areas of low attenuation (resembling a recent infarct) or slit-like lesions, with or without evidence of calcification.

In Table II, the appearances of the lesions seen on follow-up are related to the location of the original haematoma. Putaminal haematomas appeared to leave more obvious residual lesions than thalamic, brainstem, or lobar haemorrhages.

Other changes

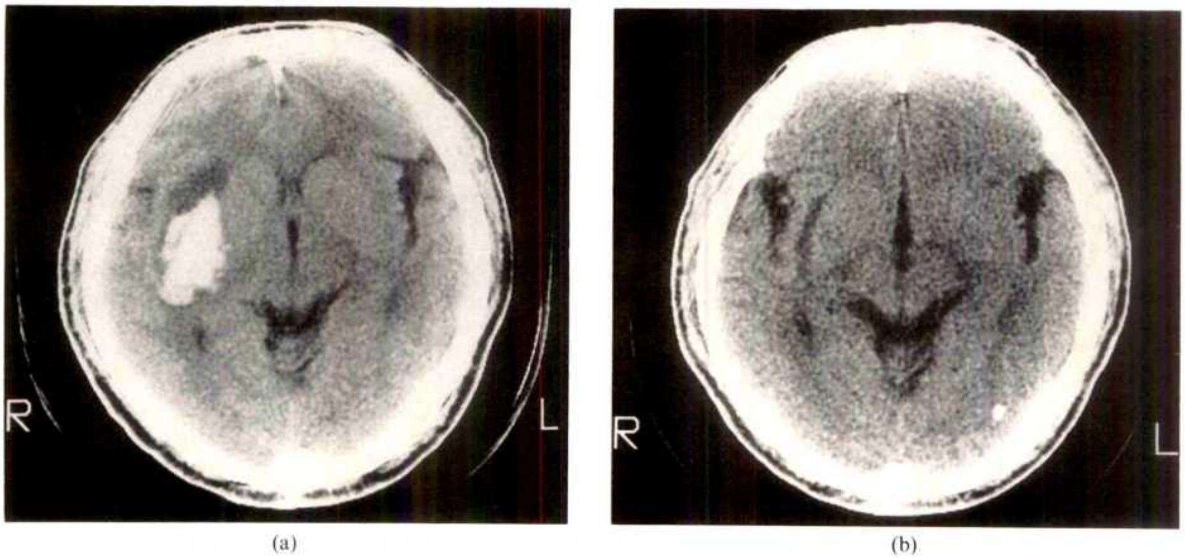
In 12 patients, initial CT showed one or two focal areas of low attenuation distant from the haematoma. All but two of these patients were hypertensive but only two had a history of previous stroke.

On follow-up CT, five patients developed one or two small areas of low attenuation in the ipsilateral corona radiata one slice above the site of haemorrhage.

Intraventricular extension of the haemorrhage was noted in the initial CT of seven patients. In six of these, there was no sign of hydrocephalus in the acute stage, nor was significant ventricular enlargement subsequently evident. However, the seventh patient, who had a mid-brain haematoma, did develop acute hydrocephalus; 3 months later there was a calcified area at the site of the haematoma but the ventricles had reverted to normal size.

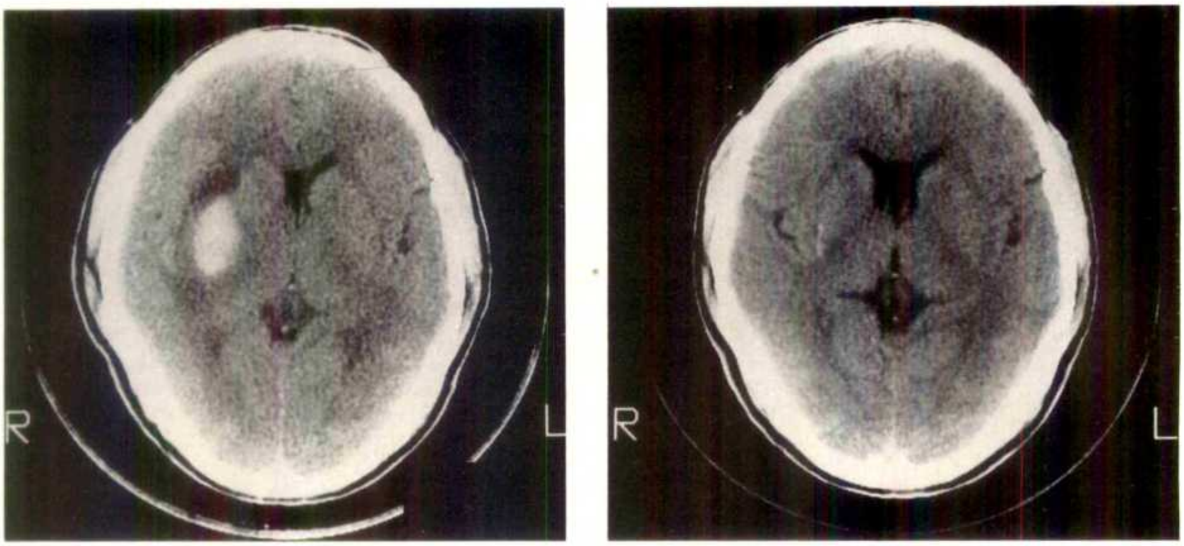
Functional assessment

All 40 patients were assessed according to the Barthel ADL Scale (maximum score = 20) at the 3 month follow-up visit. 30 (75%) were functionally independent, with a score of 19 or 20. Five (12%) were mildly disabled, with a score between 16 and 18. The remaining five (12%) were significantly disabled, with a score of 15 or less. In Table III, the appearances of the lesions seen on follow-up are shown in relation to functional status. There was an inverse correlation ($r = -0.35$, $p < 0.05$) between the size of the residual lesion on CT and the Barthel score. Moreover, as shown in Table IV, nine of



(a) (b)

Figure 1. CT of a 48-year-old male. (a) Shows a rounded haematoma measuring 4 × 2 cm in the right putamen. (b) 3 months later, a slit-like low density lesion remains, measuring 4 cm in length.



(a) (b)

Figure 2. CT of a 49-year-old male. (a) Shows a rounded haematoma measuring 3.5 × 2 cm in the right putamen. (b) 3 months later, a calcified slit remains, measuring 1.3 cm in length.

the 10 patients who were disabled (Barthel score of 18 or less) showed either evidence of previous cerebrovascular disease ("old infarct") on the initial CT, or the emergence of a new ischaemic lesion ("new infarct") in an area adjacent to the original haematoma on the follow-up CT. In contrast, only eight of the 30 patients with a Barthel score of 19 or 20 showed any sign of "old" or "new" ischaemic lesions.

Table I. CT appearances of follow-up lesions and size of original haematoma

Follow-up CT appearance	Number of patients	Mean original size (cm)	Range (cm)
Complete resolution	11	2.95	0.8–5.1
Low attenuation—minimal	4	1.58	1.0–1.8
Low attenuation—0.6 to 1.5 cm	4	3.25	1.5–4.0
Low attenuation—1.6 to 2.5 cm	7	4.04	3.5–5.0
Calcification	4	3.63	2.3–5.1
Slit-like lesion < 2.5 cm	5	2.76	2.0–4.0
Slit-like lesion > 2.5 cm	5	4.96	3.3–7.0
Total	40		

Table II. CT appearances of follow-up lesions and location of original haematoma

Follow-up CT appearances	Number of patients	Putamen	Thalamus	Brainstem	Lobar	I–V*
Complete resolution	11	1	4	3	2	1
Low attenuation—minimal	4	1	2	1	0	0
Low attenuation—0.6 to 1.5 cm	4	2	2	0	0	0
Low attenuation—1.6 to 2.5 cm	7	3	3	0	1	0
Calcification	4	1	1	1	1	0
Slit-like lesion	10	10	0	0	0	0
Total	40	18	12	5	4	1

* I–V = Intraventricular

Table III. CT appearances of follow-up lesions and functional status of patient 3 months after primary intracerebral haemorrhage

Follow-up CT appearances	Number of patients	Independent	Mild disability	Significant disability
Complete resolution	11	10	0	1
Low attenuation—minimal	4	3	1	0
Low attenuation—0.6 to 1.5 cm	4	2	1	1
Low attenuation—1.6 to 2.5 cm	7	5	0	2
Calcification	4	3	0	1
Slit-like lesion < 2.5 cm	5	5	0	0
Slit-like lesion > 2.5 cm	5	2	3	0
Total	40	30	5	5

Table IV. Functional status and presence of "old" or "new" ischaemic lesions on follow-up computed tomography

Functional status	Number of patients	Patients with Old infarct	Patients with New infarct
Independent	30	6	2
Mild disability	5	1	3
Significant disability	5	5	0
Total	40		

Discussion

By including every patient admitted with acute stroke, without prejudice of age and clinical condition, we showed that 31% of 388 strokes in our Chinese population were the result of PICH. This agrees closely with the figure of 30.6% reported recently by Huang et al (1990) in Hong Kong Chinese and is more than twice the quoted percentage (12–14%) in Caucasians (Sandercock et al, 1985; Fieschi et al, 1988; Rowe et al, 1988). 53% of our patients with PICH died within 3 months. 40 of the 56 survivors (71%) were studied with follow-up CT. The 16 survivors not studied included two who were too disabled to attend (Barthel scores, obtained over the telephone, of 4 and 11, respectively) and two who declined repeat scanning (both had Barthel scores of 20). The remaining 12 patients either had moved away (8) or were staying in a nursing home (4). Patients who did return for follow-up CT were otherwise not selected in any way and there is no difference in mean initial haematoma size between them and those who did not return (3.26 cm and 3.48 cm, respectively, $p = 0.60$). Thus, 71% of survivors were re-scanned and we believe these were representative of all survivors in this series.

There are few comparable studies in the literature, and none in Chinese patients. In an Italian follow-up CT study of 69 PICH patients surviving at 1 year, Fieschi et al (1988) noted that 26% had a poor clinical recovery. Follow-up CT showed a focal low density area in 70%, no appreciable defect in 20%, a "porencephalic cavity" in 7% and calcification in only 3%. In an earlier Danish study of 29 patients with follow-up CT (Helweg-Larsen et al, 1984), 16 (55%) were described as having normal neurological examination, seven (24%) minor sequelae and six (21%) debilitating sequelae. Follow-up CT showed low density or "focal atrophy" or both in 72%, normal appearances in 10%, "porencephaly" in 10% and calcification in 7%.

The present study involved 40 patients with follow-up CT, of whom 10 (25%) were disabled 3 months after the PICH. This is similar to the 26% and 21% found in the Italian and Danish series, respectively. On the follow-up CT, a higher percentage of our patients had no lesion (27% *vs* 20% and 10%) and a smaller proportion showed plain low densities only (37% *vs* 70% and 72%). Slit-like linear lesions, presumably due to collapsed porencephalic cysts, and calcifications were observed more commonly than described previously. The reason for this is unclear, but it may reflect, in part, the resolution of different generations of CT scanners.

Knowledge of the various long term CT manifestations of PICH is important for diagnostic accuracy, especially when patients prone to cerebrovascular disease are being studied. Since nearly a third of haematomas resolve almost completely, normal CT does not exclude previous haemorrhage. Slit-like lesions, especially those lying deep in the basal ganglia, are probably reliable markers of previous haematoma. On the other hand, rounded or irregular areas of low attenuation can be caused by previous haemorrhage or recent infarct, and clinical information will be necessary to tell the difference. Although a distinct feature in some cases, calcification is not specific to previous haemorrhage and may be found in a variety of non-vascular intracerebral conditions.

The size of the initial haemorrhage has been shown to be a predictor of mortality and morbidity (Hier et al, 1977; Kwak et al, 1983). In the present study of survivors only, the size of the residual lesion also correlated with the degree of residual disability; although the association was not close. Follow-up CT showed not only residual areas of low attenuation at the site of haemorrhage, but in five cases there were additional lesions of similar attenuation nearby. These new low attenuation areas may represent secondary infarcts due to ischaemia or oedema sustained during the acute stage of haemorrhage. The occurrence of such secondary infarction may explain why some patients did not recover as well as others with a similar initial haematoma.

In summary, we have shown that in Hong Kong Chinese patients admitted to hospital with acute stoke, PICH accounted for approximately one third of cases, of whom slightly more than half died within 3 months. Of the 40 survivors studied, three quarters were functionally independent and one quarter showed varying degrees of disability at 3 months. Follow-up CT showed no residual lesion in 27%, low attenuation areas in 37%, slit-like lesions in 25%, and calcification in 10% of these patients. The size of the residual lesion correlated weakly to the degree of residual disability.

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The chest X ray in Q-fever: a report on 69 cases from the 1989 West Midlands outbreak

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Abstract. Acute and serial chest radiographic appearances of Q-fever in a large UK outbreak in the West Midlands are described. In 69 acute films (taken within 20 days of onset of illness), 10% of films were normal. Appearances in 62 abnormal films were varied and, in contrast to some previous reports, showed no features that might distinguish Q-fever pneumonia from pneumonias of other origins. Analysis of serial films in 47 cases showed that complete radiographic resolution frequently took up to 6 months, longer than has been described previously. Initial appearances deteriorated over the first 2 weeks of radiographic surveillance in 20% of cases. No relationship was found between the extent of radiographic change and the age of the patient or the presence or absence of respiratory symptoms. Age did not affect time to resolution.

Q-fever, first described by Derrick in 1937 (Derrick, 1937), is most commonly manifest as an acute febrile illness often with pneumonic features. World-wide in distribution, most cases in the UK occur amongst those occupationally exposed to cattle and sheep, the main animal reservoir of *Coxiella burnetii*. Infection is most commonly caused by inhalation of an aerosol of dust contaminated with *Coxiella* organisms which are found in the highest concentrations in the birth products of infected animals. An acute febrile illness follows an average incubation period of 20 days (Sawyer et al, 1987); pneumonic features are common and complete recovery is usual, although some cases may become protracted. A small number of cases of acute Q-fever may go on to develop chronic *Coxiella* infection manifest as microbiological culture negative endocarditis, hepatitis or osteomyelitis (Fergusson et al, 1985). A typical radiographic appearance has been described as consisting of a few roughly rounded, homogeneous consolidations in both lungs, with plate atelectasis being a common finding (Sutton, 1987).

In May 1989, the largest reported UK outbreak of Q-fever occurred in the West Midlands involving 147 recognized cases, the majority of whom had no occupational risk of acquiring the infection (Hawker et al, 1991; Smith et al, 1991). We have reviewed the acute chest radiographic appearances in 69 of the cases and assessed serial films in 47 of these.

Methods

In early May 1989, general practitioners and hospital doctors in Solihull and surrounding areas of the West Midlands became aware of an excess number of cases of pneumonic illness occurring in young men. Screening for antibodies to *Coxiella burnetii* proved positive in a large number of cases. Subsequent investigation by clinicians, microbiologists and community physicians identified 147 cases of Q-fever with a peak incidence in the first week of May, the majority (82%) of cases occurring over a 5 week period. Full details of the epidemiological and clinical features of this outbreak are to be published elsewhere (Hawker et al, 1991; Smith et al, 1991). Details available in 129 cases (88% of all cases) revealed that 83 (64.3%) patients were admitted to 20 different hospitals, 30 (23.3%) patients were seen in eight hospital outpatient departments and 16 (12.4%) patients were managed wholly in the community by 16 general practitioners. We endeavoured to identify and obtain all chest X rays performed by the various physicians on these patients in the course of their illness. In addition, a number of films were obtained at special Q-fever clinics held at East Birmingham Hospital 6 months after the outbreak (November 1989) to which all identified cases were invited. Basic demographic data and information concerning presenting symptoms were also obtained for each patient.

Radiographs were assessed in two ways. Firstly, acute chest radiographs, defined as those taken within 20 days of the onset of symptoms were identified. Secondly, cases with two or more films giving the opportunity to study serial changes were identified. Acute films were viewed and scored separately by two experienced observers using a standard scoring scheme that assessed shadowing according to site, extent and nature. The presence of other features was also noted. Where opinions differed, films were reviewed jointly and a

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consensus agreed. Serial films were assessed in the same way. Demographic and clinical data relating to each case were analysed by the χ^2 method using appropriate contingency tables.

Results

Acute radiographs

69 chest radiographs taken within the first 20 days of illness were obtained and reviewed. This represented 83% of those known to be admitted to hospital. Two of these films were mass miniature radiography (MMR) films, four were antero-posterior and the remaining 63 were postero-anterior radiographs. In the remaining 78 patients, no clinical details were available for 45 patients, no radiography was performed within the first 2 weeks of illness in 15 patients and films, although requested, were not forthcoming for the remaining 18 patients. The mean interval (SD) between date of onset of symptoms and date of film was 6.1 (4.2) days, range 0–20. 60 (87%) cases were male. The mean age (SD) of the patients was 45.5 (13.2) years, range 21–77. This demographic pattern was similar to that seen in the outbreak group as a whole ($n = 147$). There was initial agreement between the observers on 88.2% of X-ray observations. Seven of the films (10%) were considered normal. The findings in the remaining 62 abnormal films are summarized in Table I. There were no characteristic features, although in general, shadowing was more likely to be unilateral (92%), affecting one (61%) or two (32%) zones, homogeneous (82%), peripheral (55%) and basal (48%). Figure 1 shows a typical appearance.

Table I. Acute chest X ray characteristics in 69 cases of Q-fever

Characteristic	Number of radiographs showing characteristic	Percentage ($n = 69$)
Normal	7	10
Abnormal	62	90
Shadowing		($n = 62$)
Unilateral	57	92
Bilateral	5	8
Number of affected zones (of six)		($n = 62$)
One	38	61
Two	20	32
Three	2	3.5
Four	2	3.5
More than four	0	0
Site of shadowing[a]		
Peripheral	34	55 ($n = 62$)
Perihilar	10	16
Segmental	13	21
Lobar	5	8
Upper zone	17	18 ($n = 92$)[b]
Middle zone	31	34
Lower zone	44	48
Left	34	60 ($n = 57$)[c]
Right	23	40
Nature of shadowing		($n = 62$)
Homogeneous	51	82
Nodular (2–4 mm)	6	10
Reticular	5	8
Ill-defined	62	100
Well-defined	0	0
Additional features		($n = 62$)
Air bronchograms	20	32
Linear atelectasis	5	8
Pleural effusions	2 (small)	3
Cavitation	0	0

[a] Where shadowing affected more than one zone unilaterally, shadowing was always in adjacent zones.

[b] $n = 92$ as more than one zone could be affected.

[c] $n = 57$ as in five cases shadowing was bilateral.

Relationship to clinical symptoms. 61 of the 69 patients reported at least one of three respiratory symptoms of cough, breathlessness or chest pain as a feature of their acute illness. Eight patients reported no respiratory symptoms (Fig. 2). Of these eight patients only one had a normal acute chest X ray. The remaining six normal films belonged to patients reporting at least one respiratory symtom (mean 1.6). 54 of the 69 patients were admitted to hospital, a further 11 were seen in hospital outpatient clinics whilst four were managed wholly in the community. Of the eight patients with no respiratory symptoms six were admitted to hospital and two seen in outpatient clinics. All the patients with normal acute films were admitted to hospital, many presenting with high fever. Statistical analysis by the χ^2 method showed no relationship between the number of zones affected and the presence or absence of respiratory symptoms or the patient's age.

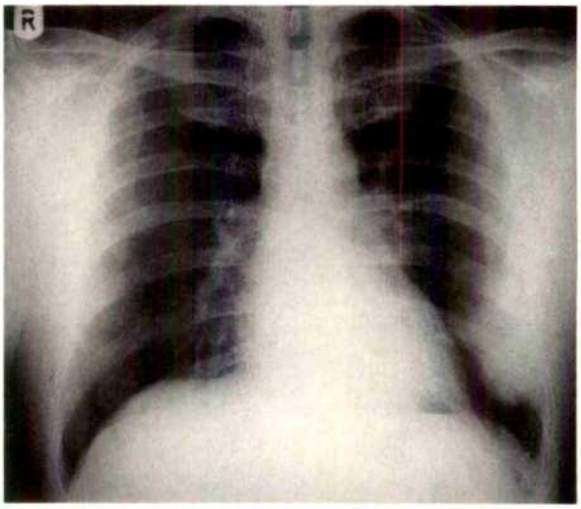
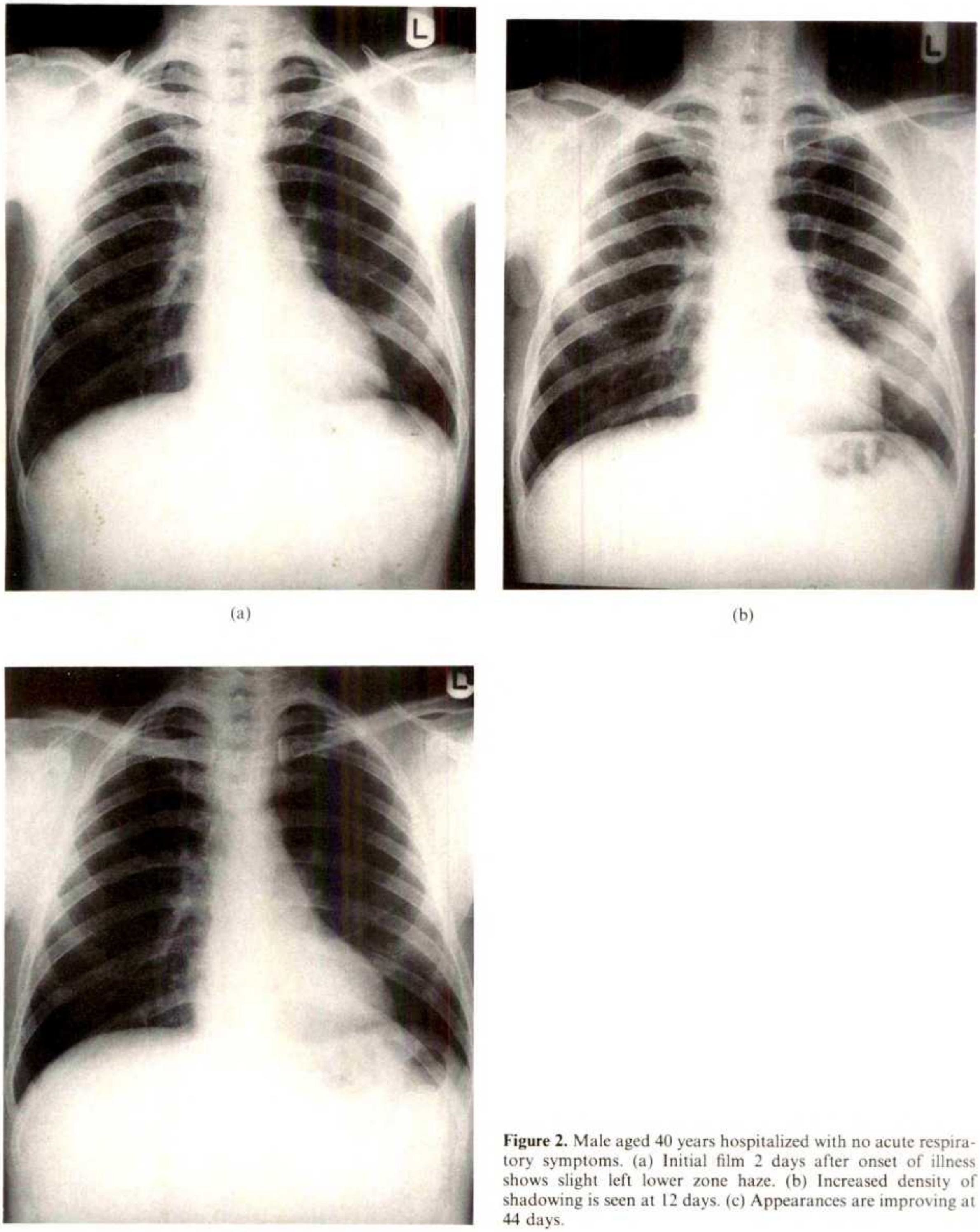


Figure 1. Male aged 42 years, presented with two out of three respiratory symptoms and was hospitalized. Film taken 5 days after onset of illness shows peripheral left lower zone homogeneous consolidation.



(a)

(b)

(c)

Figure 2. Male aged 40 years hospitalized with no acute respiratory symptoms. (a) Initial film 2 days after onset of illness shows slight left lower zone haze. (b) Increased density of shadowing is seen at 12 days. (c) Appearances are improving at 44 days.

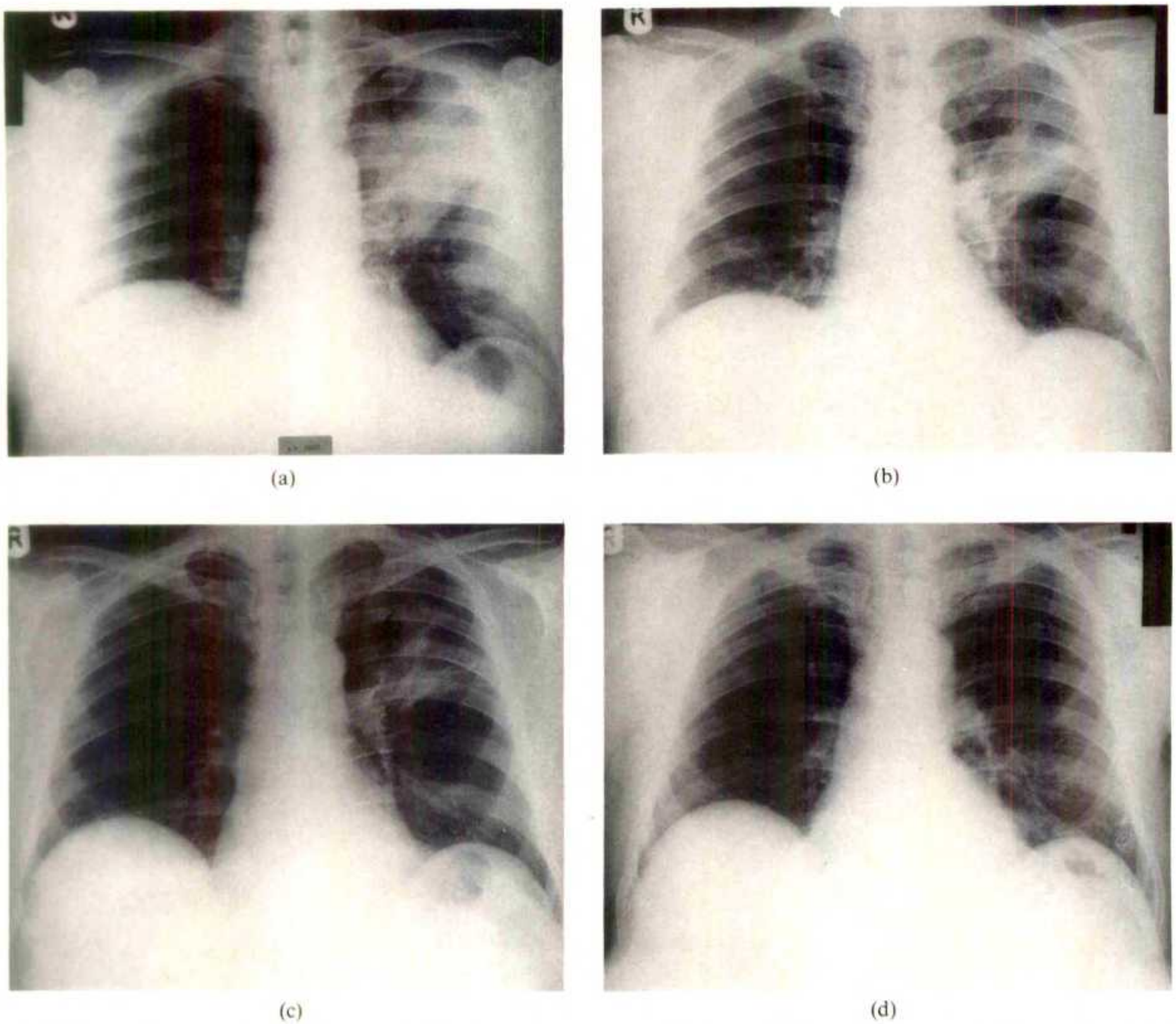
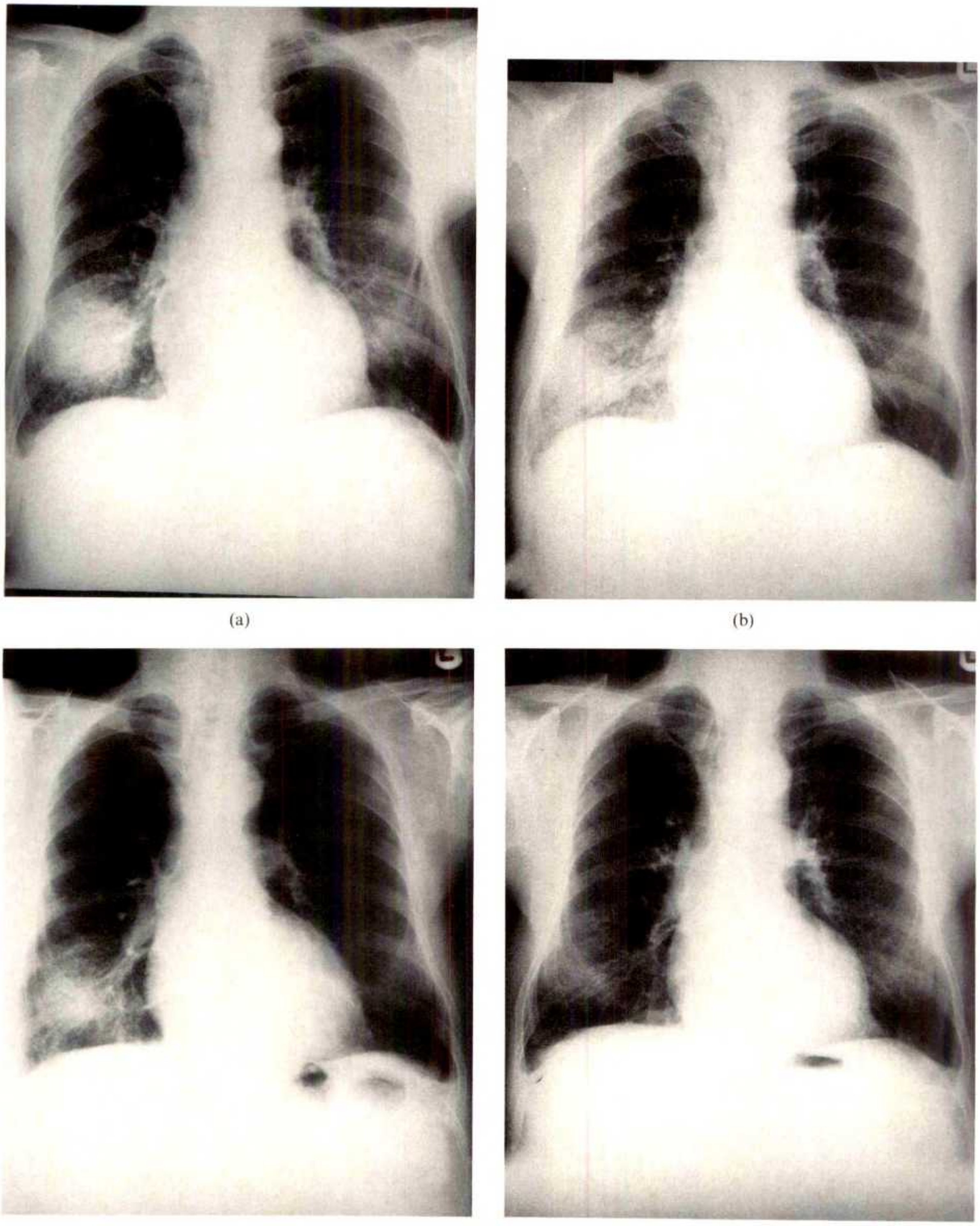


Figure 3. Male aged 60 years, hospitalized with two respiratory symptoms. (a) Initial film 7 days after the onset of symptoms shows left sided upper and mid-zone homogeneous shadowing with an air bronchogram. (b) There is an initial rapid improvement at 11 days. (c) Further improvement is seen at 23 days with a degree of atelectasis. (d) Complete resolution was seen at 163 days.

Serial films

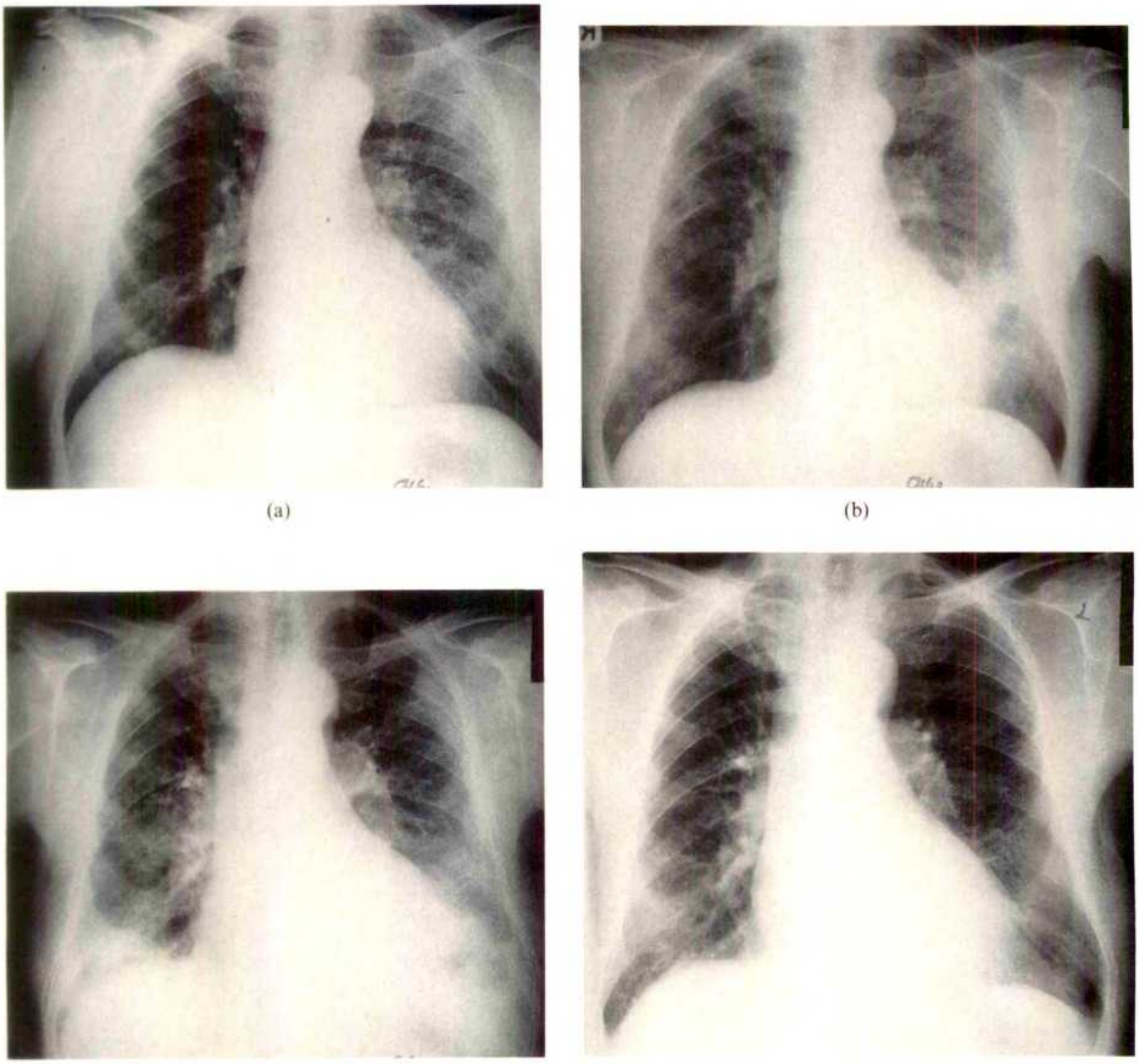
In 47 cases, of which 41 (87%) were male, 176 serial films were reviewed. Serial films for the remaining patients were not performed in 22 cases, not forthcoming on request in 33 cases and clinical details were unavailable for the remainder. The mean age (SD) of these 47 patients was 47.3 (12.3) years, range 27–75. The average number of films taken in each case was 3.7, range 2–6. In 26 cases the chest radiograph was noted to have returned to normal (Fig. 3), while in the remaining 21 cases the last available film was still considered abnormal (Fig. 4), although all were improving. In 10 film series there was initial worsening of appearances (Figs 2, 4 & 5). In all but one of these, appearances deteriorated within 2 weeks of the initial film before improvement was seen. The time course of normalization or improvement of these films is summarized in Fig. 6.

Relationship to clinical symptoms. Six of the 47 serial cases reported no respiratory symptoms with their acute illness. In all but one of these cases serial films returned to normal, one by 3 months and the remainder by 6 months. Statistical analysis by the χ^2 method revealed no relationship between age and time to resolution in the 26 cases in which complete resolution was seen. There was also no relationship found between the presence of symptoms and time to resolution. However, there was a significant relationship between time to resolution and hospitalization ($p < 0.04$), the films of those patients who were hospitalized taking longer to resolve completely.



(a) (b) (c) (d)

Figure 4. Male aged 65 years hospitalized with one respiratory symptom. (a) Initial film, 2 days after onset of symptoms, shows a peripheral rounded right lower zone shadow. (b) There is increased, more diffuse shadowing at 6 days. (c) Improvement is seen by 10 days. (d) There is persisting streaky shadowing at the right lower zone at 148 days.



(a) (b)

(c) (d)

Figure 5. Male aged 63 years was hospitalized with two respiratory symptoms. (a) Initial film 2 days after onset of illness shows diffuse shadowing in the left lung and the right lower zone. (b) At 23 days there is worsening of the left sided shadowing. (c) At 65 days the right sided changes have worsened and a pleural effusion is seen on the left. (d) At 107 days appearances have improved bilaterally with resolution of the pleural effusion.

Discussion

Previous reports of the chest X ray appearances of Q-fever have suggested useful distinguishing features which might prompt correct diagnosis before results of serological investigations are available. For instance, Millar (1978) reviewing 32 chest X rays, suggested that the presence of plate atelectasis was helpful as a distinguishing feature from primary atypical pneumonia in some cases. Gordon et al (1984) reviewing 25 cases, 14 sporadic and 11 occurring in a localized outbreak, suggested differences in appearances of chest X ray abnormalities between their two groups of patients; the epidemic cases showed a higher incidence of rounded and multiple shadows than the sporadic group.

There may be some bias in the patients we consider here, the majority having been admitted to hospital and, thus, more likely to have been X rayed than those managed in the community. These patients have, by definition, more severe illness, but the sample in this radiographic survey are representative of the outbreak group as a whole with respect to age and sex profiles, although the proportion admitted to hospital is slightly

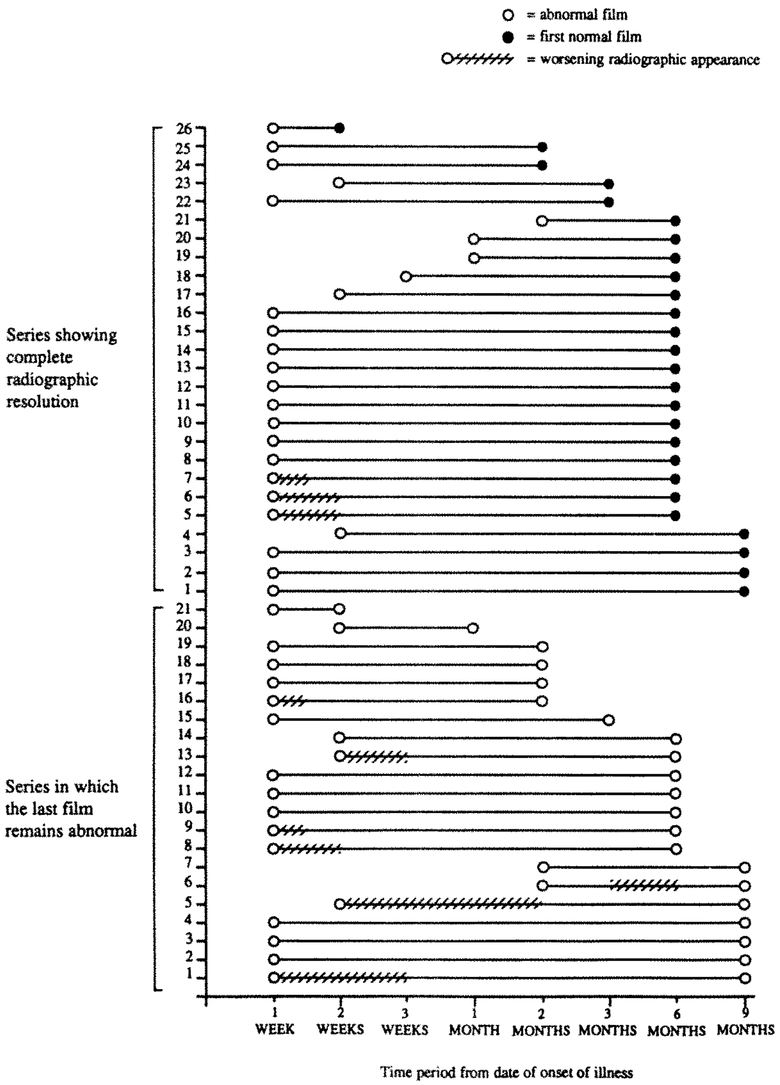


Figure 6. Time course of resolution of chest X ray abnormality in 47 cases of Q-fever, with 26 series showing complete resolution and 21 series with persisting radiological abnormality.

higher (78%) than that seen in the outbreak group as a whole (64.3%). Because of the retrospective nature of this study and the large number of institutions involved in the care of these patients, clinical practice with regard to timing of X-ray investigations was not consistent. A significant number of patients were not followed radiographically to complete resolution. This does not necessarily imply that resolution did not occur, only that continued radiographic follow-up was not considered necessary by the clinician involved.

With these limitations in mind we feel this study reflects a wide spectrum of radiographic appearances in Q-fever. Our results show that the acute radiograph may be normal, even in the presence of respiratory symptoms. Moreover, radiographic abnormalities may be present in the absence of respiratory symptoms. When present, shadowing has a predilection for the lower zones and occurs more commonly on the left. However, any zone of the lung may be affected. Shadowing is uniformly ill defined, largely homogeneous and tends to be peripheral. Air bronchograms may be present in up to a third of cases, but linear atelectasis is less common and pleural effusions are rare, contrary to previous series (Millar, 1978; Gordon et al, 1984). We found no evidence on the acute chest radiograph to distinguish Q-fever pneumonia from pneumonias of other aetiologies.

Our study of serial changes shows that complete radiographic resolution may frequently be delayed for up to 6 months and in some cases longer. Appearances may deteriorate in the first 2 weeks of radiographic observation. There appears to be no correlation between the duration of resolution and age or presenting symptoms, but the duration of resolution was longer in those patients admitted to hospital.

Acknowledgments

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The value of repeated chest radiographs in the follow-up of patients with germ cell testicular tumours

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Abstract. Patients with germ cell testicular tumours customarily have repeated follow-up chest radiographs after treatment. This study assesses the contribution of chest radiography to the detection of recurrent disease in 162 patients. Six patients developed an intrathoracic recurrence, but in only one case was the chest radiograph the only indication of recurrence. Five had other evidence to suggest recurrence, such as raised serum markers or palpable masses. The yield from follow-up chest radiographs in patients with germ cell testicular tumours is very low and their use must be balanced against both the harmful effects of radiation and the financial cost.

Although testicular tumours are uncommon, with an average incidence of 3.5 per 100 000 males per year (IARC, 1987), they are important for two reasons. Firstly, they are the most common malignancy of young men and secondly, with current treatment regimes, a high cure rate is possible even with disseminated disease. It is widely recognized that these patients require follow-up for long periods after treatment. The current Medical Research Council protocols require frequent chest radiographs for follow-up. It is sometimes felt that the number of these is excessive. However, there is little published data relating specifically to their value in the follow-up of patients in remission. This study assesses the contribution of chest radiographs in the detection of disease recurrence in patients with germ cell testicular tumours.

Patients and methods

The clinical records of 183 patients with testicular teratomas and seminomas who were referred to the Hogarth Centre of Radiotherapy and Oncology between December 1981 and December 1988 were reviewed. Four patients were excluded from the study as their records were incomplete.

After treatment 162 patients were in complete remission. This was defined as no clinical, serum marker (alphafetoprotein (AFP), beta-human chorionic gonadotrophin (B-hCG)) or radiographic evidence of disease for at least 1 month. The diagnosis of germ cell tumour was confirmed histologically. 90 had primary testicular seminomas, 70 primary testicular teratomas and two extragonadal teratomas. Mixed tumours were analysed as teratomas.

The mean age of the patients was 35 years (range 18–79 years). The mean follow-up period was 4 years 8 months. Only three patients were followed-up for less than 1 year.

Patients were staged according to the widely used Royal Marsden Hospital staging classification. Initial staging consisted of postero-anterior and lateral chest radiographs, lymphogram, serum markers, and, since 1984, computed tomography (CT) examination of the thorax, abdomen and pelvis. Before the introduction of CT, staging included whole lung tomography and abdominal ultrasound.

Subsequent follow-up studies followed current Medical Research Council (MRC) protocols. The frequency of chest radiographs is shown in Table I.

Results

Of the 162 patients, relapse occurred in 18 (11.1%). Six patients developed recurrence in the thorax (Tables II & III). Of the three with teratoma, all initially had Stage I disease which was treated by orchidectomy. All three had raised serum AFP levels at the time recurrence was demonstrated. Recurrence was seen on the chest radiograph in two of these patients and on CT in the third.

Three patients with seminoma, initially Stage II, developed recurrence in the thorax. One developed a mass in the left supraclavicular fossa, associated with raised serum B-hCG levels. CT examination demonstrated para-aortic and mediastinal lymphadenopathy. Despite further treatment this patient died of uncontrolled disease. The second patient developed a painful chest wall mass 16 months after orchidectomy, which biopsy confirmed to be metastic seminoma. The serum

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Table I. Frequency of chest radiograph following treatment

Teratoma Stage I	
First year	monthly
Second year	2 monthly
Third year	3 monthly
Thereafter	6 monthly
From MRC Testicular Tumour Working Party, September 1987.	
Metastatic teratoma	
First year	2 monthly
Second year	3 monthly
Third year	4 monthly
Fourth year	6 monthly
Thereafter	annually
From MRC Urological Cancer Working Party, testicular tumour subgroup, Protocol June 1989.	
Seminoma Stage I	
First year	3 monthly
Second year	4 monthly
Third year	6 monthly
Fourth and fifth years	annually
From MRC Urological Cancer Working Party, testicular tumour subgroup, March 1989.	

B-hCG level was not elevated. This patient also developed metastases in the right iliac crest and liver. The third patient developed an asymptomatic mediastinal recurrence 13 months after orchidectomy and abdominal irradiation (Fig. 1). Serum B-hCG levels were not elevated. A routine follow-up chest X ray was the only indication of recurrence in this patient.

Table II. Staging of patients who had recurrence of tumour

Stage	Number of patients	Number of relapses
Teratoma		
1	38	9
2	19	0
3	3	0
4	12	1[a]
Seminoma		
1	65	3
2	23	5
3	1	1
4	1	0

[a] Original tumour extragonadal.

Discussion

The majority of testicular tumours occurring below the age of 50 years are of germ cell origin, comprising teratomas, seminomas and combined tumours. The combined tumours are treated as a subgroup of teratoma for the purposes of management. Approximately 75% of germ cell tumours produce serum markers. Teratomas may produce either or both of the markers AFP or B-hCG. Pure seminomas do not secrete AFP but may secrete B-hCG (Logothetis, 1990).

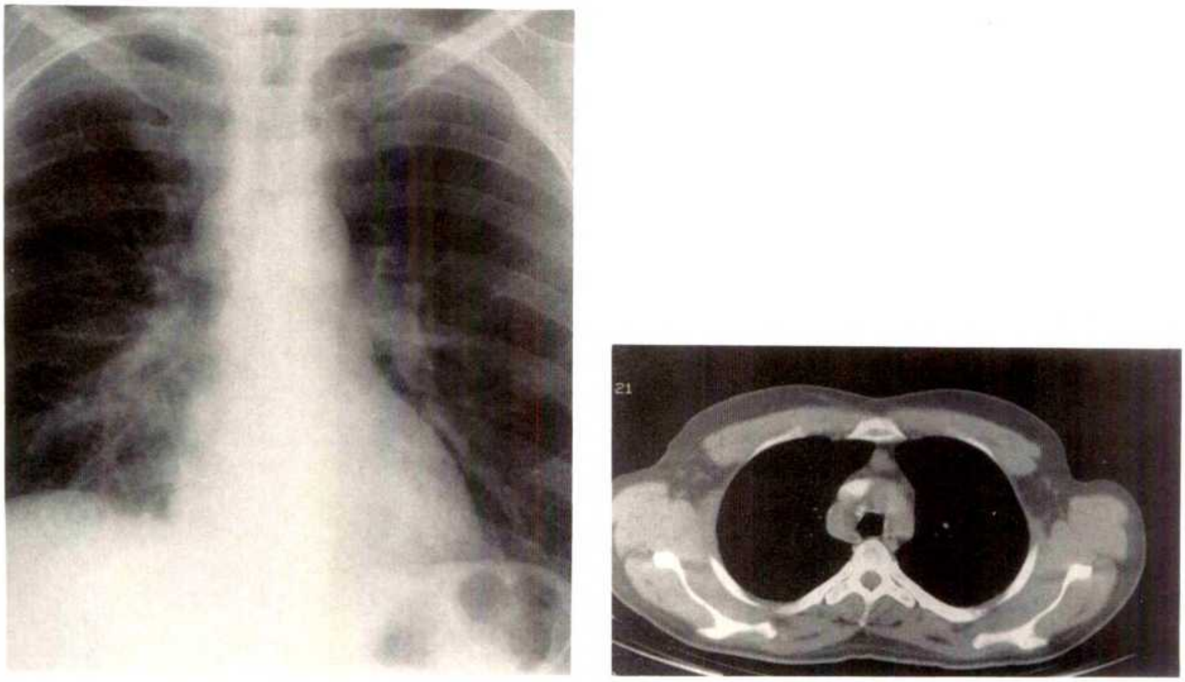
The majority of teratoma recurrences are detected by elevation of serum marker levels (Freedman et al, 1987). Rising levels of serum markers are often the first sign of relapse and may precede demonstration of radiographic or clinical recurrence by several months (Grigor et al,

Table III. Details of patients who had recurrence of tumour

Patient	Histology	Initial stage	Time to relapse (months)	Site of relapse
1	Sem	2	16	Thorax
2	Sem	2	13	Thorax
3	Sem	2	6	Thorax, RP, SCF
4	Sem	1	76	RP
5	Sem	3	48	RP
6	Sem	1	6	RP
7	Sem	2	12	RP
8	Sem	1	14	RP
9	Sem	2	10	SCF
10	MTU + Sem	1	3	Thorax, RP
11	MTI	1	13	Thorax
12	MTU + Sem	1	4	Thorax
13	MTU	1	20	RP
14	MTI	1	8	RP
15	MTI	1	8	RP
16	MTU + Sem	1	3	RP
17	MTI	1	6	Inguinal ring
18	MTU	4[a]	9	RP

RP = retroperitoneum, SCF = supraclavicular fossa, MTU = malignant teratoma undifferentiated, MTI = malignant teratoma intermediate.

[a] Extragonadal.



(a) (b)

Figure 1. (a) Postero-anterior radiograph showing widening of the superior mediastinum caused by recurrent seminoma. (b) A CT scan of the same patient confirms the presence of a right paratracheal mass.

1977; Lange & Fraley, 1977). Serum markers are less reliable in the detection of recurrence of seminoma (Horwich et al, 1985).

Most patients treated for seminoma remain disease free. If recurrence occurs it tends to be within the initial areas of disease (Logothetis et al, 1987) although, in this study, four of the nine patients who relapsed after treatment for Stage II seminoma had recurrences at other sites as well (Cases 1, 2, 3, 9).

Disease recurrence is commonest in patients with Stage I teratoma. Recurrence rates of about one-quarter occur in series where Stage I teratoma has been treated by orchidectomy alone (Freedman et al, 1987). The commonest site of recurrence is the retroperitoneal lymph nodes followed by the thorax. A high risk group of patients with Stage I disease who are most likely to relapse can be identified by various histological features of the primary tumour (Hoskin et al, 1986). These patients may now be treated with two courses of chemotherapy after orchidectomy. In this study all patients with thoracic recurrence of teratoma had rising serum markers at the time recurrence was demonstrated. One patient (Case 12) had a pulmonary mass which was confirmed as a metastasis by percutaneous needle biopsy. He was treated with chemotherapy and his serum markers returned to normal although the mass continued to enlarge. The mass was excised and histology showed only mature teratoma. The presence of residual masses which continue to enlarge after chemotherapy, but are composed of mature teratoma only, has been described previously as the "growing teratoma syndrome" (Logothetis et al, 1982; Panicek et al, 1990). The pathogenesis of this is uncertain, but possible mechanisms suggested include selective death of the more rapidly dividing malignant cells or chemotherapy induced differentiation of the existing malignant elements (Hong et al, 1977; Oosterhuis et al, 1983; Panicek et al, 1990).

The objective of repeated chest radiographs and serum marker estimations in the follow-up of patients with germ cell testicular tumours is to detect low volume recurrence and thereby improve the chance of cure (Bredael et al, 1983). The risk of not performing regular chest radiographs is that large asymptomatic lung metastases might develop, requiring, at the very least, longer courses of chemotherapy than would have been necessary if the metastases had been smaller or less numerous (MRC, 1985).

Lung metastases from teratomas are often seen without mediastinal involvement. However, seminomas tend to metastasize via lymphatics, so mediastinal disease is often seen in the absence of lung metastases. If lung metastases are present with seminomas they are usually associated with mediastinal involvement (Husband, 1990).

Chest radiographs are not a sensitive method of detecting pulmonary recurrence. Lung metastases may be present on CT or whole lung tomography which are not seen on plain radiographs (Williams et al, 1987a; Lein et al, 1988). Chest radiographs are particularly insensitive in detecting mediastinal recurrence, which is common in recurrent seminoma (Husband & Grimer, 1985; Williams et al, 1987b). Although in this study the only patient with recurrence detected solely by follow-up chest radiographs, had a mediastinal recurrence of seminoma.

The radiation dose from repeated chest X rays is low, especially when compared with the radiotherapy dose some patients receive during the course of their treatment. For example, in most centres patients with Stage I seminoma receive prophylactic abdominal irradiation (3000 cGy). However, those with teratomas will not be treated with radiation therapy and their only exposure will be associated with staging and follow-up. We calculated that the average dose equivalent each patient received over the study period from follow-up chest X rays was 2.25 mSv. However, radiation dose is cumulative and this is in addition to the radiation exposure each patient will receive from other investigations. Patients with testicular tumours are usually young and, with current treatment regimes, fertility is usually preserved. The risks of carcinogenesis and mutagenesis from follow-up chest radiographs may be low (NRPB, 1990), but if these investigations make no positive contribution to the clinical management of the patient, it is difficult to justify their present frequency.

Uncontrolled recurrent tumour was the cause of death in two of our patients (Cases 3 and 18). In neither did routine follow-up chest radiographs contribute to the diagnosis of recurrence. At the time of writing, we were entering our patients in the MRC studies which define the frequency of chest radiographs. However, on the basis of this review we would recommend at least doubling the intervals between routine chest radiographs, although serum markers should continue to be checked at regular intervals. By reducing the frequency of routine follow-up chest radiographs savings can be expected.

An exception to this general recommendation of reducing the frequency of routine chest radiographs will be in the relatively rare marker negative teratoma. These patients are easily recognized at presentation and schedules as currently defined by the MRC are appropriate.

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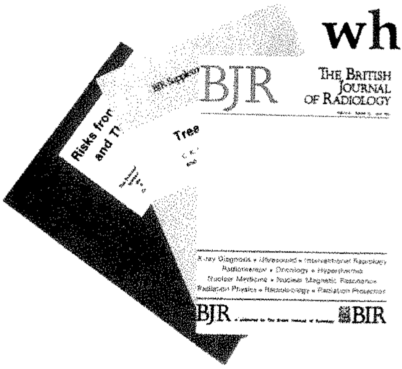

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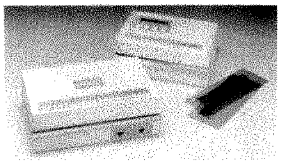

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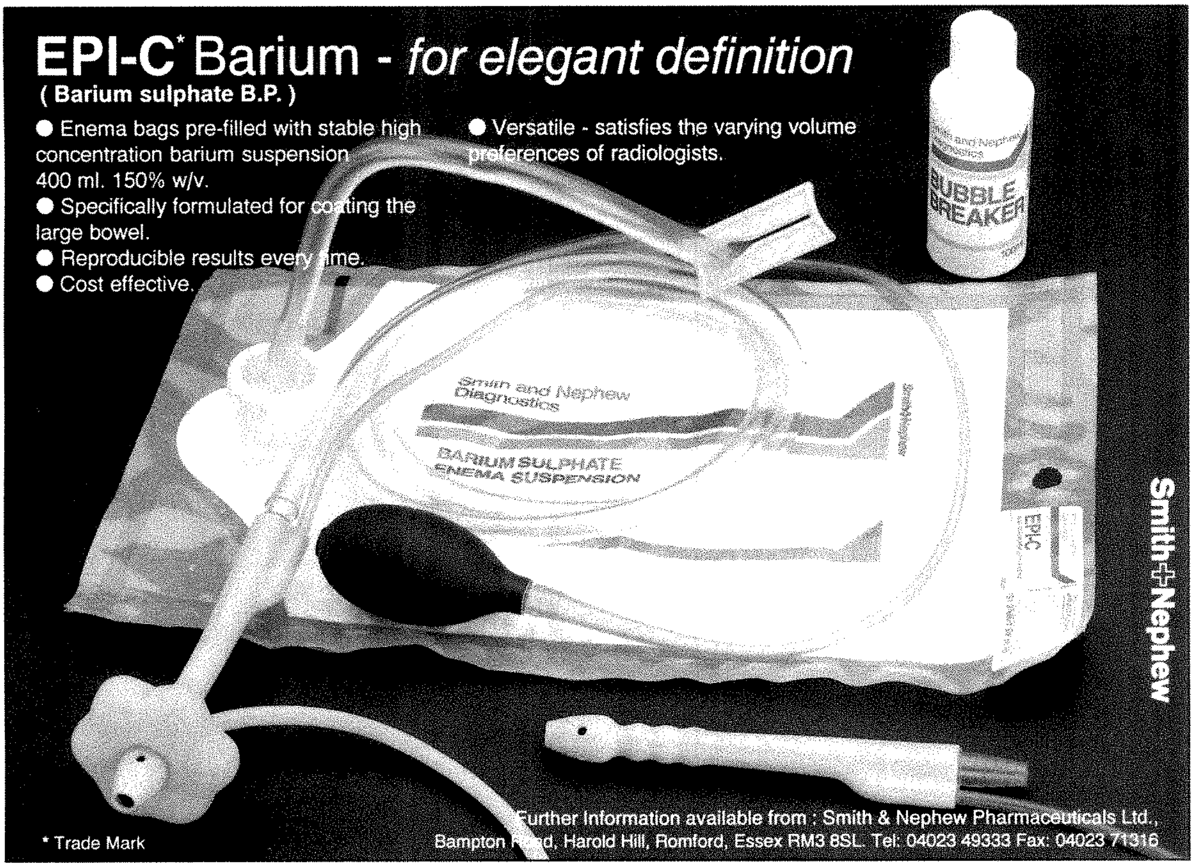

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Chronic stress injuries of the elbow in young gymnasts

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Abstract. The radiological changes of chronic stress injuries of the elbow in 19 adolescent elite gymnasts are reported. The principal abnormalities were avascular necrosis of the capitellar epiphysis (Panner's disease) (one patient), post-traumatic subarticular necrosis (osteochondritis dissecans) of the capitellum (six patients) and the medial articular eminence of the distal humerus (one patient). Flattening and anterior depression of the radial head epiphysis with an underlying metaphyseal notch associated with an epiphyseal cleft (three patients), which, in one patient who continued training, developed into a chronic Salter Type IV stress fracture. A further patient, post-epiphyseal fusion, showed osteochondritis dissecans of the anterior aspect of the radial head. Seven patients exhibited a spectrum of olecranon changes from fragmentation of the epiphysis to chronic Salter Type I stress fractures of the growth plate. A follow-up survey found that, of those who responded to a questionnaire, nearly all the patients with articular surface damage failed to continue with competitive gymnastics whereas those with olecranon abnormalities were able to continue gymnastics at the same level. The mechanism of injury and the pathological changes are discussed.

Musculoskeletal injuries, both acute and chronic, are a well recognized hazard of gymnastics (Goldberg, 1980). Elite gymnasts have been shown to have delayed skeletal maturation (Malina, 1983) resulting in a skeleton susceptible to overuse injuries (Maffulli, 1989). During many gymnastic routines such as tumbling and vaulting the upper limb bears weight and is subject to the type of injuries usually found in the lower limbs. The distal radial growth plate of adolescent gymnasts is prone to chronic stress injuries (Auberge et al, 1984; Carter et al, 1988; Fliegel, 1986; Roy et al, 1985), and the purpose of this paper is to report the radiographic appearances of chronic stress injuries of the elbow joint in adolescent gymnasts.

Patients

19 gymnasts between the age of 6 and 18 years (mean 13.5 years) were seen with chronic stress injuries of the elbow resulting from training. There were 14 males and five females. All trained for between 4.5 and 10 h per week. Rheumatological conditions were excluded. Antero-posterior and lateral radiographs of the elbow joint were obtained at presentation in all cases. Follow-up radiographs were available in 14 cases (length of follow-up 0–120 months; mean length of follow-up 18 months; mean number of radiographic examinations 4.7).

The radiographs were reviewed and the appearances of the elbow injuries recorded. Clinical follow-up consisted of a postal questionnaire regarding current symptoms, the ability to continue with sports and competitive gymnastics, and any residual functional deficit. Responses were received from 70% of the patients with the remainder untraceable.

The radiographs of a further series of patients consecutively presenting to a casualty department with acute elbow trauma were reviewed to estimate the prevalence of non-acute radiographic abnormalities in the "normal" population.

Results

The principal radiographic abnormalities were confined to the capitellum (seven patients), the head and neck of radius (four patients), the medial articular eminence of the distal humerus (one patient) and the olecranon epiphysis (seven patients).

Abnormalities of the capitellum

In one patient avascular necrosis (Panner's disease) was indicated by sclerosis, irregular margin and fissuring of the capitellar epiphysis. The remaining six cases, all post-fusion of the capitellar growth plate, showed varying degrees of osteochondritis dissecans from rarefaction of the subarticular bone proceeding to cyst formation and fragmentation of the articular cortex (Figs 1 and 2). The abnormalities were bilateral in four of the five cases in which both elbows were radiographed. Intra-articular loose body formation was subsequently identified in five of the 11 affected elbows (Fig. 1b, c). Progression of the radiographic signs was relatively slow, but in no cases did healing occur with restoration of normal appearances. In four cases there was thickening of the articular cortex of the adjacent

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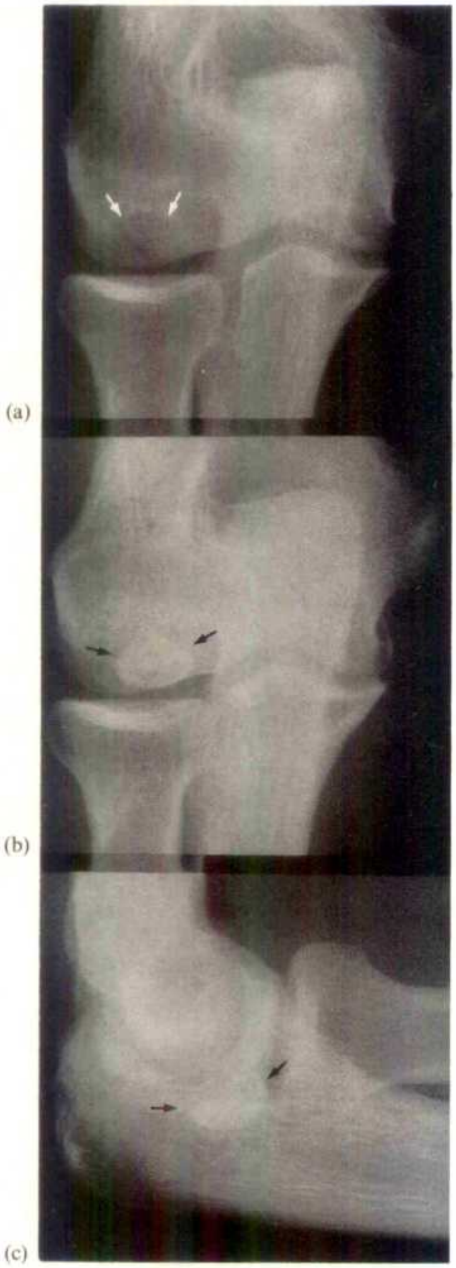


Figure 1. Osteochondritis dissecans of the capitellum indicated by rarefaction of the subarticular bone (a) (arrowed) and progressing to loose body formation 4 years later (b, c) (arrowed).

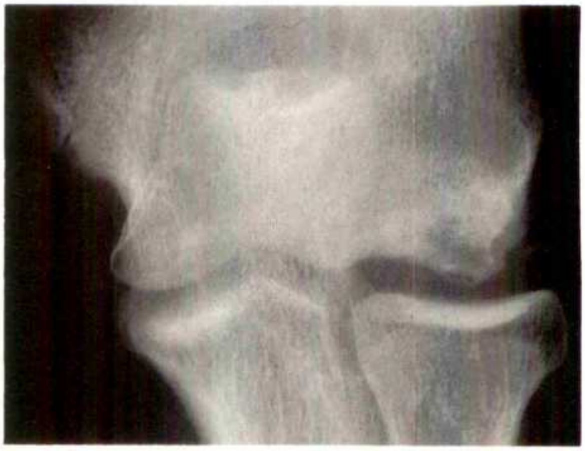


Figure 2. Osteochondritis dissecans of the capitellum indicated by subarticular cyst formation and fragmentation of the articular cortex. Sclerosis of the articular cortex of the radial head in response to stress.

radial head in response to stress (Fig. 2) and in one case narrowing of the radiocapitellar joint indicated premature degenerative joint disease.

Abnormalities of the radial head and neck

Radiographs of both elbows were available in all four cases. Bilateral asymmetrical abnormalities of the radial head and neck were present in three cases. In two of the younger patients the first abnormality was flattening of the radial head epiphysis with anterior depression (Fig. 3a). Subsequently, a cleft appeared in the antero-lateral aspect of the epiphysis with an underlying metaphyseal defect best seen on the over-rotated antero-posterior view (Fig. 3). One of these patients, who continued intensive training, developed marked fragmentation (Fig. 4), and ultimately, 10 years after presentation, a large antero-lateral exostosis with posterior subluxation of the radial head. This was surgically excised. A further patient, who presented after fusion of the radial head epiphysis, showed a defect in the anterior radial head with overlying fragmentation and subsequently loose body formation (Fig. 5). The fourth case had a cleft epiphysis with an underlying metaphyseal defect affecting the postero-medial portion of the radial head, which healed with a medial metaphyseal spur and loose body formation.

Abnormality of the medial articular eminence

The radiographs in one 17-year-old male gymnast revealed fragmentation and underlying cystic change of the medial articular eminence, which divides the trochlea from the capitellum (Fig. 6a). This area of presumed osteochondritis dissecans healed with hypertrophy of the articular eminence and formation of a discrete loose body (Fig. 6b).

Abnormalities of the olecranon epiphysis

All seven cases showed widening of the growth plate and/or fragmentation of the epiphysis (Fig. 7). In two cases, a band of irregular mineralization, indicative of a stress fracture, developed in the widened growth plate (Fig. 7). Two cases eventually required internal fixation of the growth plate to relieve persistent symptoms. Two

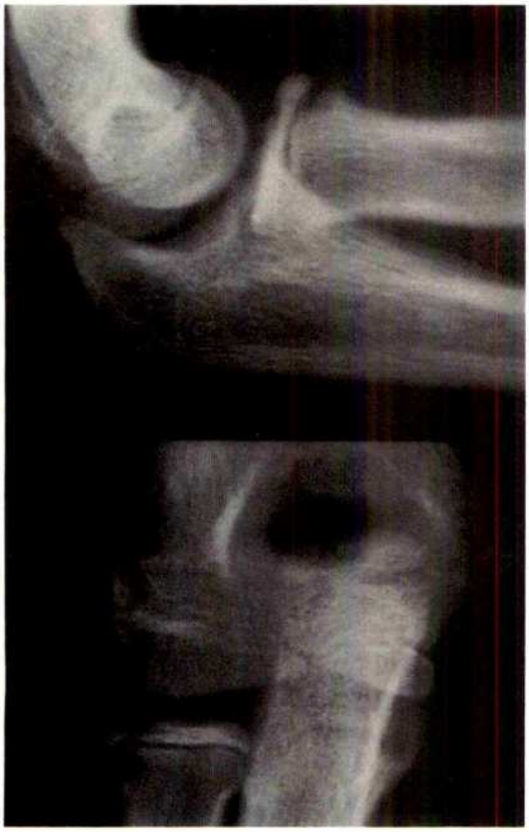


Figure 3. Chronic stress induced anterior depression of the radial head with an underlying metaphyseal defect on the lateral radiograph (a) and a lateral epiphyseal cleft on the antero-posterior radiograph (b).

of this group also had radiographic evidence of chronic stress changes of the distal radial growth plate.

Clinical outcome

Of those patients with articular changes detailed above, only one of the eight who responded to the questionnaire was able to return to competitive gymnastics. By contrast, the patients with olecranon epiphyseal changes had a more satisfactory outcome in that all who returned the questionnaire were able to return to competitive gymnastics.

"Normal" population

The radiographs of 320 patients with acute elbow trauma, but otherwise unselected, were reviewed. Skeletal fusion had not taken place in 15%. Excluding acute traumatic abnormalities, the following changes were identified. In the children: a wide olecranon growth plate in one case, fragmentation of the olecranon epiphysis in one case, anterior depression of the radial head in one case and irregularity of the trochlear epiphysis in one case. In the adult patients: ununited ossification centres or old avulsion injuries of the medial epicondyle were identified in four cases and lateral epicondyle in one. Cystic changes were present in the capitellum in one case, loose bodies without obvious sites of origin in two and olecranon traction spurs as part of degenerative joint disease in five.

Discussion

Intensive training and a high pain threshold in top class athletes frequently leads to overuse injuries. The gymnast bears weight on the upper limb during manoeuvres such as handstands, tumbling, one-arm

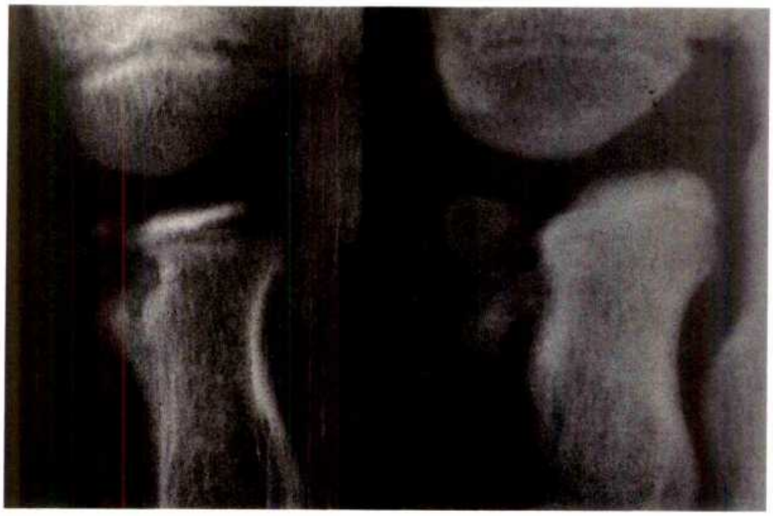


Figure 4. Over-rotated antero-posterior radiograph showing a lateral epiphyseal cleft with a prominent underlying metaphyseal defect (a). Two years later, the radial head is dysplastic with disordered ossification laterally (b).

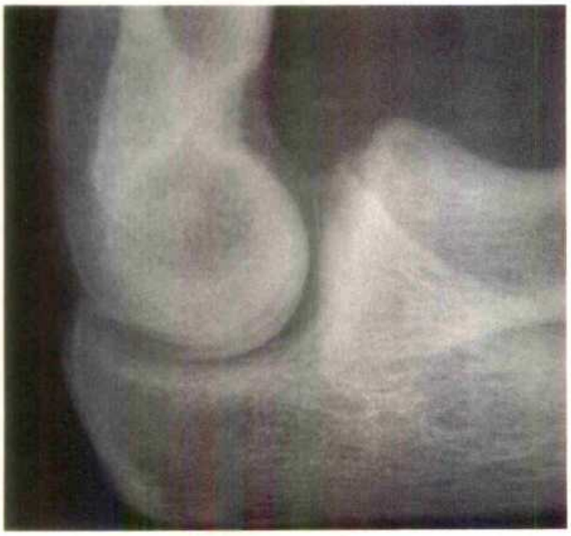
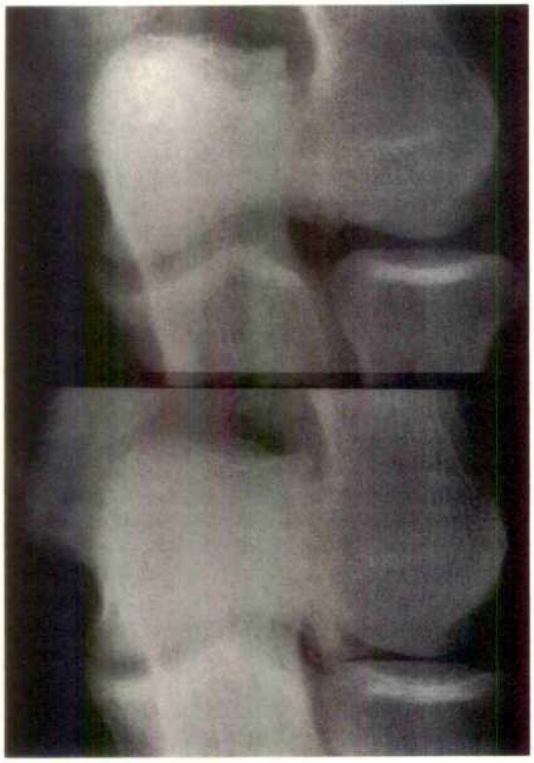


Figure 5. Osteochondritis dissecans of the radial head indicated by the defect in the anterior aspect with an overlying ossific fragment.



(a)

(b)

Figure 6. Osteochondritis dissecans of the medial articular eminence of the distal humerus indicated by fragmentation and subarticular cyst formation (a). Four years later, healing has occurred with hypertrophy of the ridge and a small loose body (b).

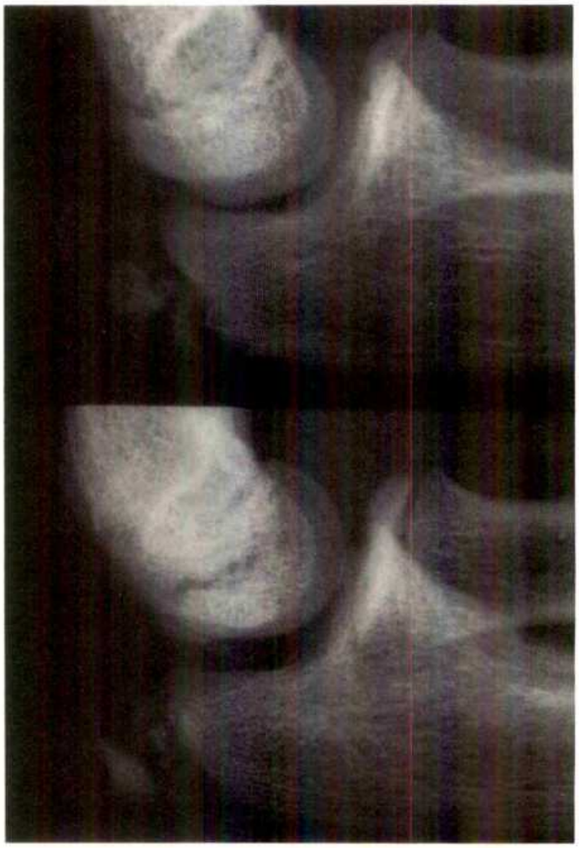


Figure 7. Two cases of Salter Type I stress fractures of the olecranon growth plate indicated by widening of the growth plate and an irregular band of ossification. Note also the anterior depression of the radial head in response to stress.

balance and trunk stabilization on the bars (Goldberg, 1980). The principal abnormal forces experienced in the elbow joint are medial torsion, lateral compression and extension stress (Slocum, 1968; Gore et al, 1980), which may ultimately result in radiographic abnormalities.

Medial-torsion-induced injuries are typically associated with sports requiring a repetitive vigorous throwing action. A classic example is the chronic avulsion or traction apophysitis of the medial epicondyle seen in baseball pitchers, part of a spectrum of abnormalities known as "Little Leaguer's elbow" (Adams, 1965; Pappas, 1982). Similar overuse injuries may be a problem for those practising racquet sports (Gore et al, 1980; Priest et al, 1974) as well as gymnasts (Goldberg, 1980). Only one of our cases exhibited a medially located lesion, the subarticular post-traumatic necrosis (osteochondritis dissecans) of the medial articular eminence (Fig. 6). In their review of the literature, the authors are unaware of any further case of a similar lesion occurring at precisely the same site, although both a prominent medial articular ridge and a paratrochlear ossicle are recognized normal variants (Kohler & Zimmer, 1968; Keats, 1988).

Lateral compression injuries of the elbow were much more common in this series. They are caused by the forced impaction of the radial head into the capitellum. With only two exceptions, the proximal radial abnormalities presented at an earlier age than the capitellar changes in this study. The reason for this age discrepancy is uncertain. Contributory factors may include the later age of appearance of the radial head ossific nucleus, alterations in the ratio of volume of ossific nucleus to non-ossified cartilaginous epiphysis (Ellman, 1975) and differences in the relative size of the radial head to the capitellum. In full elbow extension, lateral compression forces act maximally on the anterior aspect of the radial head, causing anterior depression (Figs 3a and 7) (Ellman, 1975). If training is continued, the excess shear forces produce chronic Salter Type IV stress fractures extending through the antero-lateral aspect of the radial head epiphysis to involve the underlying metaphysis (Figs 3 and 4).

Epiphyseal clefts have been described at numerous sites (Harrison & Keats, 1980), including the radial head, and are generally considered normal variants as are lateral notches of the proximal radial metaphysis (Silberstein et al, 1982; Keats, 1988). Obviously the changes in this series are of pathological significance (Figs 3 and 4). It is interesting to speculate whether these so-called normal variants represent a *forme fruste* of lateral compression injuries to the radial head, albeit of no clinical significance. The radial head lesion presenting at the same site, after epiphyseal fusion, shows appearances typical of subarticular post-traumatic necrosis (osteochondritis dissecans) (Fig. 5). In one case, the postero-medial location of the epiphyseal cleft and underlying metaphyseal defect is unusual but not unknown for osteochondrosis (Keats, 1990).

The capitellum was the equal commonest site of abnormality in this series. In the initial stages of ossification, usually before 11 years of age, avascular necrosis (Panner's disease) may occur, as in the youngest gymnast in this group. At this age the capitellar epiphysis is supplied by one or two separate vessels (Singer & Roy, 1984) entering the epiphysis posteriorly, which are vulnerable to lateral compression owing to repetitive valgus stresses. At a slightly older age, during the adolescent growth spurt, the capitellum is susceptible to subchondral fractures, also attributed to chronic stress, which may progress to subarticular post-traumatic necrosis (osteochondritis dissecans) and loose body formation (Figs 1 and 2). Such abnormalities are recognized in gymnasts (Priest & Weise, 1981; Singer & Roy, 1984; Jackson et al, 1989) as well as sports involving repetitive throwing (Pappas, 1982), the use of a racquet (Gore et al, 1980) and in BMX riding where at least 40% of the weight of the rider is borne by the arms (Fixsen & Maffulli, 1989).

Explosive extension of the elbow by the triceps muscle is required in gymnastics for balancing and tumbling routines (Aronen, 1985). This exerts both traction and shearing forces on the olecranon when the elbow locks in extension. These excess forces may produce abnormalities at two sites in the patient before skeletal fusion: firstly, at the musculotendinous insertion of the triceps into the olecranon and, secondly, the olecranon physis. Acute avulsion injuries are well recognized, but traction epiphysitis is uncommon, with isolated cases attributed to gymnastics (Danielsson et al, 1983), baseball (Francis et al, 1978), hockey (Danielsson et al, 1983) and diving (Hunter & O'Connor, 1980). The radiographic appearances of fragmentation (Fig. 7) are similar to the apophysitis of the tibial tuberosity (Osgood-Schlatter's disease), but the diagnosis should be made with caution as the olecranon epiphysis usually ossifies from two or more centres (Silberstein et al, 1981; McCarthy & Ogden, 1982).

The diagnosis is less contentious when the changes affect the physis with widening followed by delayed or absent closure of the growth plate. As the space between the early ossifying olecranon epiphysis and the adjacent metaphysis may be up to 5 mm in the normal child (Silberstein et al, 1981), it may be difficult to diagnose chronic stress widening in the younger age group. By the age of 12 years the growth plate is typically relatively narrow, with serpiginous yet congruent borders such that abnormal widening is radiographically easier to detect.

Stress fractures of the olecranon growth plate are recognized (Retrum et al, 1986; Torg & Moyer, 1977) and have been described in baseball pitchers (Torg & Moyer, 1977), a wrestler (Weiss & Sawyers, 1990) and a gymnast (Wilkerson & Johns, 1990). The mechanism of action is thought to be a fatigue or stress Salter Type I fracture of the growth plate in response to chronic repetitive extension forces. Not only is the growth plate pulled apart, but also temporary localized ischaemia will prevent cartilage calcification. The proliferation of uncalcified cartilage will further contribute to the apparent widening of the growth plate. A confirmatory sign is the presence of an irregular band of ossification within the growth plate (Fig. 7) resulting from disordered mineralization. The appearances are analogous to the Salter Type I stress fractures that may occur in the distal radial growth plate of adolescent gymnasts (Carter et al, 1988), which were also present in two of the current cases with extension injuries of the olecranon.

The review of the series of patients presenting to a casualty department with an acute elbow injury revealed a low prevalence of radiographic changes not attributable to the acute trauma. While the number concerned was insufficient to determine accurately the prevalence of various changes in the normal population, sufficient differences in the highly selected group of gymnasts were apparent to confirm that in the latter patients the changes were a true reaction to chronic stress. Available responses to a questionnaire indicated that those with an olecranon lesion were able to return to competitive gymnastics whereas those with articular changes were left with a residual deficit.

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Quantitative lymphoscintigraphy using $^{99}Tc^m$ human serum albumin in patients with previously treated uterine cancer

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Keywords: $^{99}Tc^m$-HSA, Lymphoscintigraphy, Lymphoedema, Uterine cancer, Radiation therapy

Abstract. To evaluate the clinical usefulness of lymphoscintigraphy using $^{99}Tc^m$ human serum albumin ($^{99}Tc^m$-HSA) in assessing lymphoedema in the lower extremities, lymphoscintigraphy was performed by subcutaneous injection of 7.4 MBq of $^{99}Tc^m$-HSA in 26 patients with uterine cancer, previously treated by operation (OP) and/or radiation therapy (RT), and in five controls. Radioactivity at the injection site in the lower extremities was counted for 3 min at 10 min (A) and at 3 h (B) after injection, and clearance of $^{99}Tc^m$-HSA was defined as $(1-(B)/(A)) \times 100(\%)$. Clearance in controls was $46.8 \pm 3.9\%$, which was significantly more than those in the other treatment groups. Clearances in patients treated with both OP and RT were less than those in patients treated with either OP or RT alone (30.1 ± 11.4 *vs.* 41.9 ± 8.9, $43.7 \pm 9.6\%$, respectively; $p < 0.01$). The clearance in legs with lymphoedema was less than those without lymphoedema in patients treated with both OP and RT (16.6 ± 7.7 *vs.* $34.9 \pm 9.3\%$; $p < 0.01$) and in patients treated with RT (33.1 ± 7.4 *vs.* $48.0 \pm 5.6\%$; $p < 0.01$). There was a significant difference between clearance in controls and clearance in non-oedematous patients' legs treated with OP and RT ($p < 0.01$). In patients treated with RT alone, radiation dose was closely correlated with $^{99}Tc^m$-HSA clearance and with the development of lymphoedema. These data suggest that lymphoscintigraphy using $^{99}Tc^m$-HSA is useful in evaluating lymphoedema and that radiation dose is one of the factors in the development of lymphoedema.

Lymphoedema, though less common than venous oedema, is a well recognized cause of chronic swelling of the legs (Browse, 1982). Oedema of the extremities is called primary lymphoedema if no causes extrinsic to the lymphatic system can be found. It can present from birth or appear later in life. Secondary lymphoedema is associated with lymphatic obstruction as a result of post-inflammatory scarring, radical surgical procedures, radiation therapy, metastatic neoplastic disease involving the regional lymphnodes and filarial infestation (Kinmonth, 1972). Lymphoedema may be secondary to venous pathology such as varicosity and deep vein thrombosis (Kinmonth, 1972). Evaluation of the lymphatic system by traditional lymphangiography can be a difficult procedure and may involve complications. In addition, oedema may be exacerbated by lymphangiography. Moreover, venography may be required in some cases to differentiate it from swelling caused by chronic venous insufficiency. There is a need for a non-invasive method which may be easily repeated, which is complication free and which assesses lymphatic flow. Radionuclides allow a non-invasive and quantitative method with such techniques as interstitial ^{131}I albumin (Hollander et al, 1961) and intralymphatic $^{99}Tc^m$-HSA (Steckel et al, 1978). We have evaluated the clinical benefits of a quantitative radioisotope method of external counting of interstitially injected $^{99}Tc^m$-HSA in patients with uterine cancer treated previously with operation and/or irradiation.

Materials and methods

Between May 1989 and September 1990, 26 patients who had undergone operation and/or irradiation to treat uterine cancer and five normal controls participated in the study. Of the 26 patients, 13 had undergone both surgery and post-operative irradiation. Six legs in four of these 13 patients developed lymphoedema. Six patients had been treated with irradiation alone. Four legs in two of the six patients developed lymphoedema. Seven patients had been treated with operation alone and none developed lymphoedema. The ages of the study participants ranged from 25 to 78 (mean, 56.5) years.

External irradiation doses in the patients who had undergone both surgery and post-operative irradiation ranged from 40 to 60 Gy (mean, 48.7 Gy). All patients treated with radiation therapy alone had been given external and high dose-rate intracavitary irradiation except for one who, with Stage IVa (FIGO) disease, was treated with 60 Gy of external irradiation to the whole pelvis. The external irradiation dosage was 40–50 Gy with whole pelvis portals and 0–20 Gy with central shieldings. The dose of the intracavitary irradiation was 20–30 Gy at point A, which is 2 cm lateral to the uterine canal and 2 cm above the lateral fornix. A dose at point B, which is 3 cm lateral to point A, was calculated by simply adding the external irradiation dose to 30% of

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the dose at point A by intracavitary irradiation. A dose at point A reflects the tumour dose and a dose at point B reflects the dose at the lateral pelvic wall (Tod & Meredith, 1953). A dose at point B, which is believed to be related directly to lymphatic damage by irradiation, was 56–69 Gy (mean, 61.5 Gy).

Using a 25 gauge needle, 0.2 ml of tracer, corresponding to 7.4 MBq of ^{99}Tc^{m}-HSA having an oval-shaped particle size of 3.8 × 15 nm (molecular weight of 66,450), was injected into the interstitial tissues of the first and second interdigital plicae. The radioactivity at the injection site was subsequently counted with a gamma camera (gamma view-H, Hitachi Co., Ltd.), with a low energy parallel hole collimator for 3 min at 10 min (A) and at 3 h (B) after injection. The clearance of the ^{99}Tc^{m}-HSA was defined as $(1-(\mathrm{B})/(\mathrm{A}))\times 100$ (%). The values of (A) and (B) were corrected for decay of the isotope. The radioactivity at 10 min was used as a baseline of the injected dose. The reason for the 10 min timing was that some patients showed bleeding from the injection sites and it took several minutes to stop this by compressing lightly with cotton. Furthermore, time activity curves at the injection sites have revealed that the difference in radioactivity at 10 min and immediately after the injection is minimal (Ohtake et al, 1983) and this difference is not clinically important. The timing of 3 h after injection was chosen for the second counting because a preliminary study on normal controls revealed that this was close to the disappearance half-time of the isotope. Until the first counting, patients remained at bed rest; after which they were invited to follow normal activity until the second counting. All patients were physically active. To compare mean figures, Welch's *t*-test or Student's *t*-test was used.

Results

^{99}Tc^{m}-HSA clearances in patients and in normal controls are shown in Fig. 1. Clearance in normal controls was significantly more rapid than those in other groups ($p < 0.01$–$p < 0.05$). Clearance in patients who were treated by operation and irradiation was significantly more delayed than in patients who were treated by either operation or irradiation alone ($p < 0.01$). There were no significant differences between clearances in patients treated with operation alone and those in patients treated with radiation alone. Clearance was more than 40% in all of the control subjects and was less than 40% in nine of the 10 oedematous limbs.

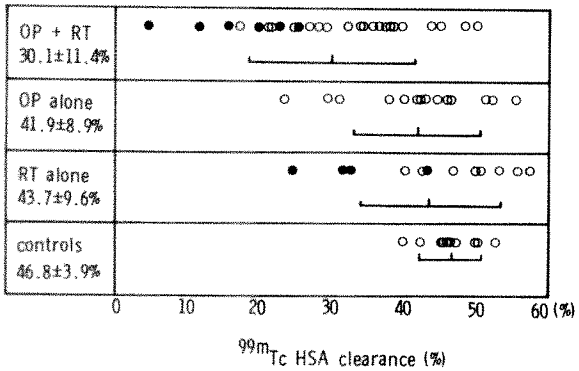

Figure 1. Clearances in various groups of treatment modalities and in controls. OP = operation; RT = radiation therapy; closed circles = with lymphoedema; open circles = without lymphoedema; OP + RT *vs.* OP: $p < 0.01$; OP + RT *vs.* RT: $p < 0.01$; OP *vs.* RT: not significant; OP + RT *vs.* controls: $p < 0.01$; OP *vs.* controls: $p < 0.01$; RT *vs.* controls: $p < 0.05$.

Table I. ^{99}Tc^{m}-HSA clearances (mean ± SD) in the presence or absence of oedema in the lower extremities

	Oedematous limbs	Non-oedematous limbs
OP + RT	16.6 ± 7.7 (n = 6)*	34.9 ± 9.3 (n = 20)**
RT alone	33.1 ± 7.4 (n = 4)†	48.9 ± 5.1 (n = 8)#
Normal controls		46.8 ± 3.9 (n = 10)# #

OP = operation, RT = radiation therapy.
* *vs.* **, * *vs.* †, * *vs.* # #, † *vs.* #, † *vs.* # #, ** *vs.* # and ** *vs.* # #: $p < 0.01$, # *vs.* # #: not significant.

Clearances in the presence or absence of lymphoedema in the same treatment groups are shown in Table I. Clearance in patients with lymphoedema was significantly more delayed than in patients without lymphoedema ($p < 0.01$). Clearance in oedematous limbs of patients treated with both operation and irradiation was more delayed than in oedematous limbs with irradiation alone ($p < 0.01$). Clearance in non-oedematous limbs of patients treated with both operation and irradiation was more delayed than in non-oedematous limbs with irradiation alone ($p < 0.01$), and in normal controls ($p < 0.01$). Clearance in non-oedematous limbs with irradiation alone was not different from that in normal controls.

In the group of irradiation alone, four legs in two patients whose point B dose was 69 Gy developed lymphoedema, whereas none of the patients whose point B doses were 60 Gy or less (56–60 Gy) developed lymphoedema. The difference of ^{99}Tc^{m}-HSA clearance in the two groups was significant ($p < 0.01$, Table I).

Discussion

Lymphoedema in the lower extremities is a common complication in the surgical or radiation treatment for uterine cancer. To assess lymphatic flow in oedematous extremities, interstitial ^{99}Tc^{m}-HSA microcolloid (37 MBq) (Weissleder & Weissleder, 1988) and ^{99}Tc^{m} sulphur microcolloid (18–20 MBq) (Carena et al, 1988) (111 MBq) (Rijke et al, 1990) have been used. The disappearance and appearance of a tracer at the draining lymphnodes and at the injection sites (time activity curves) has been analysed together with lymphoscintigraphic images. Quantitative parameters derived from the clearance data are useful to determine the grading of lymphoedema and more useful than film images in the diagnosis of lymphoedema (Weissleder & Weissleder, 1988). Film images, on the other hand, are preferable in cases where the pattern of activity distribution in the affected extremity is diagnostic, such as dermal backflow, traumatic lymphocoele, or megalymphatics (Rijke et al, 1990).

In Japan, ^{99}Tc^{m} sulphide colloid or rhenium colloid has been used clinically for lymphoscintigraphy, but there are no radiopharmaceuticals available at present for this purpose. We investigated the clinical usefulness of the method of external counting of interstitial ^{99}Tc^{m}-HSA in patients with previously treated uterine cancer and in normal controls. ^{99}Tc^{m}-HSA is a physiological substance with a particle size of 3.8 × 15 nm. The most ideal radionuclide for lymphoscintigraphy is ^{198}Au colloid with a particle size of about 5 nm and the optimal size of radiocolloids measures 3–8 nm in diameter (Strand & Persson, 1979). Smaller particles are cleared mainly through the pores of the blood capillaries; larger particles do not permeate through blood or lymphatic capillaries (Strand & Persson, 1979). The size of ^{99}Tc^{m}-HSA is close to the optimal size and can be used for lymphoscintigraphy (Ohtake & Matsui, 1986; Nawaz et al, 1990). To reduce the absorbed dose at the injection sites, lymphnode, liver, etc. and to make the study as simple as possible, we injected subcutaneously 7.4 MBq of ^{99}Tc^{m}-HSA and assessed the disappearance of the radionuclide from the injection site. With this small amount of ^{99}Tc^{m}-HSA, lymphoscintigraphic images could not be obtained.

This study demonstrated that interstitial ^{99}Tc^{m}-HSA clearance over 40% was believed to be normal. Non-oedematous patients, in whom clearance was less than 40%, were considered to have subclinical damage to the lymphatics. The clinical significance of this subclinical damage is not yet fully understood.

Clearance in oedematous legs in the operated and irradiated group was delayed more than that in the irradiated group. This may be caused by the fact that the grade of lymphoedema in the operated and irradiated group was more marked than that in the irradiated group. Clearance may be an indicator of the degree of lymphoedema, as shown by Weissleder & Weissleder (1988).

Clearance of the operated and irradiated group was most delayed. This finding suggests that effects of irradiation on the lymphatics are highest when combined with operation. This study also demonstrated that radiation therapy plays an important role in the development of lymphoedema and that radiation dose at point B is an especially important factor. There are few reports on the radiation effects on the lymphatics, although an experimental study has demonstrated that lymphatic vessels themselves are radioresistant (Engeset, 1964; Sherman & O'Brien, 1967). Radiation-induced connective tissue fibrosis impairs the patency of both lymphatic and venous channels and gives rise to both lymphatic and venous obstruction, with the development of lymphoedema (Moss et al, 1979). Radiation-induced lymphoedema is, therefore, mainly caused by connective tissue fibrosis, and is different from that resulting from direct lymphatic damage at operation. This difference might be one of the reasons why the clearance in the irradiated group in oedematous limbs was more rapid than that in the operated and irradiated group.

In conclusion, lymphoscintigraphy using interstitial ^{99}Tc^{m}-HSA is useful for quantitatively evaluating the oedematous and non-oedematous limbs, and radiation therapy, especially the dose at point B, is an important factor in the development of lymphoedema in patients treated with operation and/or irradiation for uterine cancer.

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Normal tissue reactions in the British Institute of Radiology Study of 3 fractions per week versus 5 fractions per week in the treatment of carcinoma of the laryngo-pharynx by radiotherapy

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Abstract. The radiobiological data obtained from a multicentre clinical trial of the British Institute of Radiology, which compared the treatment of carcinoma of the laryngo-pharynx by 3 fractions per week (3F/wk) with 5 fractions per week (5F/wk) radiotherapy, have been studied. The trial involved an intake of 734 patients between 1966 and 1975. The number of fractions, overall treatment time and total doses used by different treatment centres ranges from 9 to 40 fractions, 18 to 70 days and 3880 to 7800 cGy, respectively. An 11–13% reduction in the total radiation dose was applied for treatments with 3F/wk as compared with 5F/wk in centres treating over 6 weeks and 3 weeks, respectively. All patients were followed for 10 years from the start of treatment. Different types of early and late normal-tissue reactions were investigated, ranging from a low percentage incidence of perichondritis to 95% for slight early reactions. Greater than 80% of the late normal-tissue reactions seen were observed within the first year after the start of treatment, and 96% were observed within the first 5 years. There was no statistically significant difference in the normal-tissue event-free rates between the 3F/wk and 5F/wk treatment groups. This finding did not differ when different major treatment centres were studied separately. For a number of end-points, α/β ratios and N- and T-exponents of a modified nominal standard dose (NSD) formula have been calculated.

A multicentre clinical trial organized by the British Institute of Radiology was set up to compare the effectiveness of 3 fractions per week (3F/wk) to that of the more conventional 5 fractions per week (5F/wk) treatment of carcinoma of the laryngo-pharynx by radiotherapy. The final results of this clinical trial, which were mainly devoted to the general clinical findings, have been reported previously (Wiernik et al, 1990). The present report analyses the normal-tissue responses of the patients treated in this trial.

The majority of information presently available on dose–time–fractionation relationships in both humans and experimental animals is based on the study of acute radiation injury and late effects manifested within a short period of follow-up. Therefore, information on late normal-tissue responses is not yet conclusive. The data presented in this paper are a compilation of the regular assessment of the normal-tissue reponses in patients entered into the BIR trial from 1 week up to 10 years after the start of treatment. However, it must be pointed out that the aim of the study was to produce no significant difference in normal-tissue reactions between the two arms of the trial (Wiernik et al, 1990), in order to make the study possible on ethical grounds. Thus, the radiobiological data that could be obtained for different levels of reaction are limited in this study.

Methods and materials

Information was obtained from those patients entered into the first clinical trial of the BIR in a study of radiotherapy for the treatment of carcinoma of the laryngo-pharynx. A total of 734 patients from 18 major radiotherapy centres in the UK were randomly allocated to the 3F/wk or 5F/wk treatment groups between January 1966 and December 1975. The randomization list of consecutive random treatment assignments was transferred to a sequence of sealed envelopes each containing the name of the treatment (3F/wk or 5F/wk) on duplicate cards. These envelopes were supplied to individual centres through the BIR. When a patient was formally entered into the trial the clinician then opened the next envelope in the sequence and allocated the patient to the treatment group written on the cards. These duplicate registration cards, which carried the specific trial number of the prospective patient, were filled in with some preliminary information at the treat-

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Table I. Number of patients allocated to different treatment regimens by treatment centre

Treatment schedule	Centre number	Number of patients: Contributed	Not treated as planned†	Total dose not reported by centre†	Eligible for dose–time analysis	Number of fractions‡ (85% range)	Overall treatment time (days)‡ (85% range)	Dose per fraction (cGy)‡ (85% range)	Maximum tumour dose (cGy)‡ (85% range)
5F/wk	11*	67	10	7	50	24–30 (25)	31–41 (32–35)	200–271 (240–253)	5600–6511 (6000–6141)
	12	14	4	1	9	20–36 (32–36)	27–50 (40–50)	183–291 (195–291)	5820–7800 (5820–6900)
	14*	68	29	5	34	20–21 (21)	27–37 (28–30)	244–276 (250–260)	5125–5800 (5250–5500)
	15	16	9	—	7	20–40 (26–40)	28–70 (28–56)	151–283 (151–234)	5550–6030 (5550–5970)
	16	8	—	—	8	28–30 (28–30)	39–44 (39–42)	200–207 (200–207)	5750–6000 (5750–6000)
	17	7	3	3	1	20 (20)	25 (25)	250 (250)	5000 (5000)
	18	3	1	—	2	15–16 (15–16)	20–21 (20–21)	350–377 (350–377)	5600–5650 (5600–5650)
	19*	23	8	—	15	20 (20)	27–30 (27–29)	282–300 (280–293)	5636–6000 (5750–6000)
	20	11	10	1	—	— —	— —	— —	— —
	21*	56	13	—	43	27–30 (30)	37–44 (39–43)	200–237 (200–223)	6000–6850 (6200–6800)
	22	8	1	—	7	30 (30)	41–43 (41–43)	209–230 (209–230)	6290–6900 (6290–6900)
	23	5	4	—	1	33 (33)	43 (43)	204 (204)	6732 (6732)
	24*	36	7	16	13	29–30 (30)	39–43 (41–43)	208–250 (208–222)	6240–7500 (6240–6675)
	25	14	8	—	6	33 (33)	45–48 (45–48)	197–205 (197–205)	6500–6760 (6500–6760)
	26	9	3	3	3	32–33 (32–33)	44–45 (44–45)	206–208 (206–208)	6650–6840 (6650–6840)
	27	15	8	—	7	30–32 (30–32)	41–44 (41–43)	203–227 (210–217)	6300–6800 (6300–6500)
	29	2	—	1	1	32 (32)	44 (44)	203 (203)	6500 (6500)
3F/wk	11*	64	4	10	50	15–18 (15–18)	30–45 (31–35)	287–368 (343–363)	4930–5469 (5130–5400)
	12	11	3	—	8	12–23 (12–22)	25–52 (25–50)	287–416 (287–408)	4896–6600 (4896–6560)
	14*	75	24	11	40	13 (13)	27–42 (28–30)	365–438 (365–400)	4690–5700 (4750–5250)
	15	9	6	—	3	12–36 (12–36)	28–84 (28–84)	200–498 (200–498)	3880–7200 (3580–7200)
	16	9	4	—	5	18 (18)	30–42 (30–42)	297–319 (297–319)	5346–5750 (5346–5750)
	17	5	1	4	—	— —	— —	— —	— —
	18	6	—	—	6	9–10 (9–10)	18–22 (18–22)	475–544 (475–544)	4530–4900 (4530–4900)
	19*	29	8	—	21	12–13 (12–13)	25–41 (28–30)	432–473 (440–458)	5210–5680 (5280–5500)
	20	9	5	4	—	— —	— —	— —	— —
	21*	55	7	—	48	18 (18)	38–43 (38–39)	300–350 (300–328)	5500–6300 (5500–5900)
	22	6	—	—	6	18 (18)	38–42 (38–42)	306–328 (306–328)	5500–5900 (5500–5900)
	23	3	1	—	2	18–20 (18–20)	39–47 (39–47)	302–315 (302–315)	5670–6040 (5670–6040)
	24*	27	2	10	15	17–19 (18–19)	37–42 (38–42)	297–334 (303–328)	5350–6300 (5460–5950)
	25	13	2	—	11	18–20 (19–20)	42–47 (45–47)	291–336 (291–315)	5700–6710 (5780–6100)
	26	9	2	5	2	20 (20)	44 (44)	292–295 (291–295)	5830–5894 (5830–5894)
	27	18	6	—	12	18–20 (18)	39–52 (39–44)	310–315 (311–315)	5580–6240 (5580–5670)
	29	3	1	—	2	21 (21)	35–49 (35–49)	293–302 (293–302)	6150–6340 (6150–6340)

* Centres contributing > 50 patients to the trial. † These were excluded from the dose–time analysis. ‡ Applied only for patients eligible for use in dose–time analysis.

ment centre. One of the cards was returned to the BIR together with a completed, pre-circulated, trial form that contained all the clinical data for entry of the patient. The other duplicate registration card was retained at the local centre for reference. In each participating centre the length of the course of treatment was a matter of choice, being based on their standard practice. A reduction in the total radiation dose was employed for treatment with 3F/wk compared with 5F/wk. This reduction was 11–13% for overall treatment times of 6–3 weeks respectively, based on the recommendation of the Working Party (Ellis et al, 1968).

Each centre also held a second block of trial forms on which the acute radiation reactions for each patient were recorded for a period of 12 weeks from the start of radiation treatment. Thereafter, the trial office sent out personalized follow-up forms to the centres, carefully timed so as to reach the centre 2 weeks before the appointment date for the 6-monthly check-up. This form was returned to the centre in relation to the annual check-ups, which were requested to be as near as possible to the anniversary of the start of radiation treatment. "Chase-up" letters were sent to the centres if forms were not returned promptly. For this long-term follow-up the same form was shuttled backwards and forwards so that the clinician completing the form knew what had been reported previously. Each time the form came back to the trials office the new data were transcribed onto a coding form for entry into the computer data file. Reactions were not scored but recorded as present or absent.

The mean age of the patients was 62.7 years (range 32–92 years). All patients had histologically proven disease and were followed-up for up to 10 years from the start of treatment. All 13 patients contributed to one centre and another eight patients from other centres were excluded from the trial for the reasons explained in the Final Report of the Fractionation Working Party (Wiernik et al, 1990). This left 713 patients eligible for analysis. The treatment schedules of patients, with the code numbers of the treatment centres, are given in Table I. The total doses, and hence the dose per fraction listed in Table I, refer to the maximum tumour doses. This represents a dose in the hot spot in the tumour area. Although a range of overall times and doses is listed in this table, for the actual analysis exact values were used, within the intervals described below.

Early reactions were recorded at 2-weekly intervals until 12 weeks after the start of treatment. The incidence of early reactions was compared in patients treated with the 3F/wk or 5F/wk schedules. For late effects, data were collected at yearly intervals until 10 years after the start of treatment. Analysis of these data was based on reaction-free rates, and the effects of the treatment schedules were compared by the method described by Mantel (1966). This method provides an actuarial estimate, taking into account the censoring of the patients, of developing a specified reaction if the patient survives for a certain period of time. This procedure was also carried out separately for the patients treated in the five major centres that each contributed more than 50 patients.

The majority of the patients (550) were treated with ^{60}Co, 147 were treated by supervoltage X rays, and 16 were treated with ^{137}Cs irradiation. Reaction-free rates were studied separately for each radiation quality.

In a separate analysis, the effects of total dose, number of fractions, dose per fraction and overall treatment time on the incidence of normal-tissue reactions were studied. The total doses used for this analysis were the maximum tumour doses. However, this information was not reported in 81 patients. In addition, there were 194 patients who did not receive the planned treatment (Table I). These patients were excluded from the present dose–time–fractionation analyses, although not from the overall survival analyses. This left 438 patients for analysis of normal-tissue reactions. Total doses and dose per fraction were grouped into 2 Gy and 0.2 Gy increments, respectively, and for certain early and late normal-tissue reactions, the percentage of patients showing an effect in each dose per fraction group was estimated.

Similarly, patients were grouped according to the total dose versus the number of fractions (N) regardless of the overall treatment time, or according to the total dose versus the overall treatment time (T) regardless of the number of fractions. These data were analysed by probit analysis (Finney, 1964) and ED_{50} values, the dose required to produce a specified effect in 50% of the subjects treated, were obtained. These ED_{50} values were used in Strandqvist-type plots. The exponents of fraction number N and overall treatment time T were obtained from these data by regression analysis. In addition, α/β ratios were calculated from the regression analysis of a plot of the inverse of the ED_{50} values against the dose per fraction.

Results

Acute reactions

The incidence of early normal-tissue reactions occurring at any time within 12 weeks from the start of radiation treatment and those in which the duration was $\geqslant 4$ weeks are given in Table II. Almost all patients (97%) showed some kind of marked acute reaction, with 95% having a mucous membrane reaction. For this reason, dose–effect curves could not be produced for these types of reactions. However, the range of numbers of patients showing ulceration or a fibrinous reaction of the mucous membranes, oedema of the mucous membrane, any type of skin reaction, and dysphagia were sufficient to enable the construction of dose–effect curves. The ED_{50} values obtained for these end-points are shown in Tables III–V. The number of patients with dose per fraction, N or T values outside the ranges quoted in these tables was too small to be included in the analysis. The dose–time dependent variables obtained from a further analysis of these ED_{50} values are summarized in Table VI. A significant T-exponent was obtained for dysphagia and for any type of skin reaction. Of the α/β ratios obtained for early normal-

Table II. Number and percentage of patients showing early normal-tissue reactions up to 12 weeks after start of treatment

Reaction	At any time (%)	⩾ 4 weeks duration (%)
Mucous membrane		
Any type	680 (95%)	566 (79%)
Ulceration or fibrinous reaction	483 (68%)	119 (17%)
Oedema	283 (40%)	126 (18%)
Any type of marked skin reaction	544 (76%)	235 (33%)
Dysphagia	445 (62%)	192 (27%)
Perichondritis	43 (6%)	11 (1.5%)
Any type of marked acute reaction	693 (97%)	600 (84%)

Table III. Variation in the ED_{50} (±SE), with dose per fraction for various acute normal-tissue reactions. The ED_{50} values refer to the maximum tumour dose (Gy)

	Type of acute normal tissue reaction			
		Mucous membrane reaction		
Dose per fraction (Gy)	Skin reaction (any type)	Ulceration or fibrinous	Oedema	Dysphagia
2.0	—	56.80±1.96	64.43±2.96	63.33±2.16
2.1	53.03±4.85†	—	—	—
2.2	—	60.47±1.70	65.19±2.75	64.60±2.26
2.4	45.57±7.18	57.25±1.60	63.04±2.91	57.11±2.69
2.6	—	48.83±1.80	63.83±4.88	48.55±3.43
2.8	46.45±6.59	54.65±2.27	—	48.50±4.99
3.0	42.61±6.63	52.31±1.55	58.45±3.24	55.49±2.30
3.2	50.29±3.75	59.73±1.49	60.53±2.79	58.19±2.02
3.4	50.75±4.63	54.16±2.17	54.85±4.11	—
3.6	—	47.81±1.79	63.22±5.33	—
3.8	—	—	—	46.42±3.18
4.0	44.19±4.80	50.20±1.88	59.90±4.03	—

— No data or insufficient data available.

† 20–68 patients were involved in estimation of each ED_{50} value.

Table IV. Variation in the ED_{50} (±SE), with fraction number of various acute normal-tissue reactions. The ED_{50} values refer to the maximum tumour dose (Gy)

	Type of acute normal-tissue reaction			
		Mucous membrane reaction		
Number of fractions	Skin reaction (any type)	Ulceration or fibrinous	Oedema	Dysphagia
12	—	49.86±3.18†	58.15±3.23	—
13	—	50.57±3.39	52.67±2.04	—
15	—	49.23±2.58	—	—
18	—	50.31±2.76	—	58.93±2.08
19	—	—	—	—
20	—	53.67±2.94	—	50.09±5.55
21	—	48.62±2.98	—	45.91±4.89
25	—	53.03±3.45	64.28±0.94	—
28	—	—	—	59.28±2.20
30	—	54.97±3.51	—	—
32	—	—	71.20±2.62	—
33	—	58.40±4.99	—	67.63±4.47

— No data or insufficient data.

† 20–68 patients were involved in estimation of each ED_{50} value.

Table V. Variation in the ED_{50} (±SE), with overall treatment time for various acute normal-tissue reactions. ED_{50} values refer to the maximum tumour dose (Gy)

Overall treatment time (days)	Type of acute normal tissue reaction	Mucous membrane reaction		
	Skin reaction (any type)	Ulceration and fibrinous	Oedema	Dysphagia
28	35.56±6.12†	46.92±4.18	62.89±4.66	—
30	—	—	—	43.99±9.25
31	41.88±5.81	49.19±5.19	64.87±5.91	—
32	—	—	—	—
33	41.73±5.33	—	63.35±5.40	51.52±5.56
34	41.10±6.73	48.28±4.69	67.21±6.20	51.26±6.18
35	—	47.98±6.85	62.72±5.29	50.58±6.80
36	49.84±4.06	—	—	—
38	—	—	—	54.65±6.04
39	47.62±4.06	46.00±5.26	60.46±2.82	—
40	43.79±5.51	44.51±7.34	65.75±6.57	59.54±5.38
41	47.06±5.65	43.34±8.72	60.84±4.91	58.30±5.17
42	57.17±2.97	50.20±5.69	64.05±4.17	62.11±6.55
44	64.43±3.40	55.21±6.04	62.53±6.37	62.74±6.55

— No data or insufficient data.

† 20–68 patients were involved in estimation of each ED_{50} value.

tissue end-points, only that for dysphagia was significantly different from zero. The *N*-exponent was significantly different from zero for two out of the four types of early reaction investigated.

Of the number of patients who suffered an early reaction lasting ≥ 4 weeks, it was thought that it would only be possible to construct dose–effect curves for end-points such as "any kind of skin reaction" or "any kind of mucous membrane reaction", which had an overall incidence of 33% and 79%, respectively. The slopes of the dose–effect curves for these two end-points were not significantly different from zero. This was possibly due to the dispersion of the data points and the fact that radiation dose might not be the only factor determining the duration of a lesion. Therefore, no correlation could be determined between total dose and fraction size, fraction number and overall treatment time for the early end-points that had a duration of ≥ 4 weeks.

Table VI. Dose–time fractionation parameters for different acute normal-tissue reactions. These values were obtained on the basis of maximum tumour dose

Reaction	α/β^{+} (Gy)	*N*-exponent†	*T*-exponent
Mucous membrane reactions			
ulceration/fibrinous	15.0±15.13	0.13±0.04*	0.06±0.18
oedema	17.20± 9.05	0.25±0.08*	−0.05±0.077
Skin reaction (any kind)	20.50±26.0	—	1.01±0.22*
Dysphagia	3.67± 1.58*	0.39±0.26	0.88±0.08*

† Uncorrected for the effects of overall treatment time.

* Significantly different from zero ($p < 0.05$).

Late reactions

A comparison of the normal-tissue reaction-free rates for all patients for any kind of late reaction, skin reaction or mucosal reaction, according to the quality of the radiation showed no significant difference ($p > 0.5$) in the incidence of late effects between patients treated with X rays from an accelerator, ^{60}Co or ^{137}Cs γ-rays.

A comparison of the reaction-free rates of all patients treated with 3F/wk and 5F/wk, for different types of late normal-tissue reaction, are shown in Fig. 1. A similar analysis was applied separately to the five centres contributing more than 50 patients each. The relevant statistics related to this analysis are summarized in Table VII. This analysis shows that for the late effects investigated, there was no significant difference between the reaction-free rates in patients treated with 3F/wk and 5F/wk.

The number and time of the first occurrence of late normal-tissue reactions, regardless of the treatment group, are shown in Table VIII. Over 60% of the patients suffered from some type of late reaction. Telangiectasia of the skin had a low incidence (4%), whereas telangiectasia of the mucous membrane occurred in 18% of patients. In all cases, telangiectasia was persistent. In some patients (3% of cases), telangiectasia was first reported as late as the 10th year after the start of radiation treatment.

An investigation of the cumulative time-related frequency of any type of late reactions showed that > 80% of these cases seen developed within the first year from the start of radiation treatment (Fig. 2). With

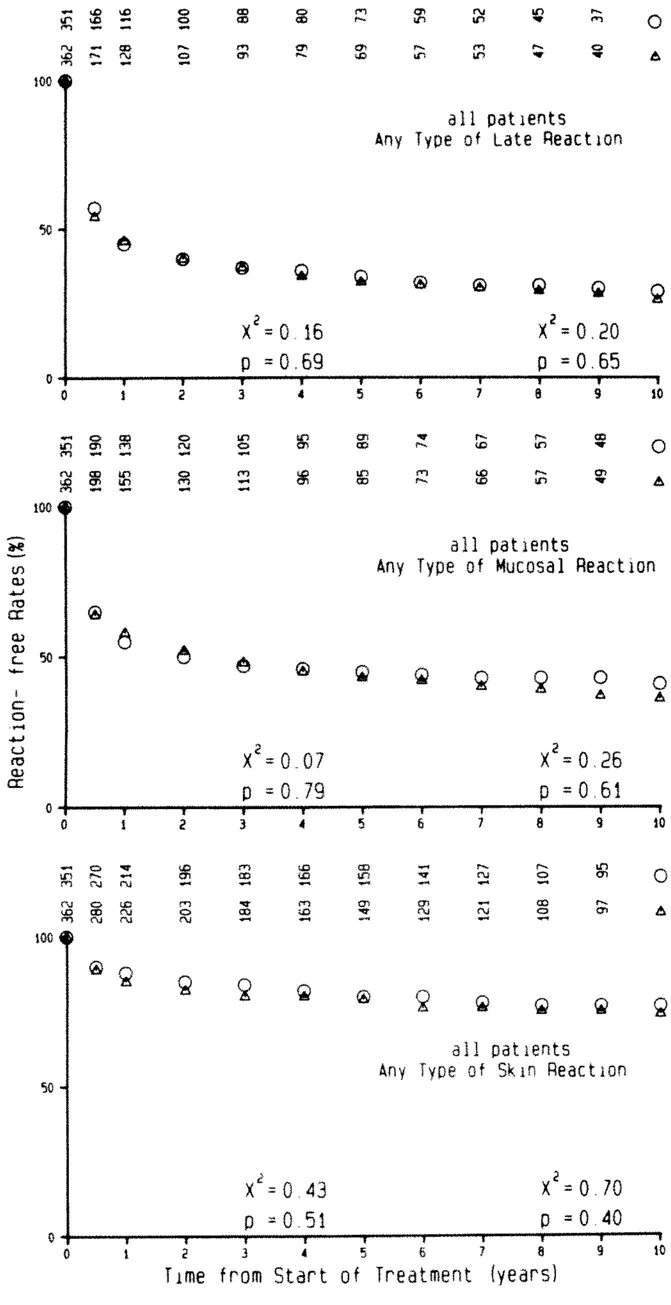

Figure 1. Reaction-free rates versus time from start of treatment for patients treated with 3F/wk and 5F/wk. The χ^2 values for time 0 up to 5 years and time 0 to 10 years from the start of treatment and the appropriate p values are given on the figure. The values of χ^2 were obtained by the method described by Mantel (1966). The numbers of patients available at the beginning of each time point are shown across the top of the figures; (○) 3F/wk, (△) 5F/wk.

the exception of telangiectasia/oedema of the mucous membrane and telangiectasia of the skin, > 60% of late reactions developed first appeared within the first year after treatment. This implies that the average latent period, the time required for the reaction to develop in 50% of the patients in whom it eventually did so (LP_{50}), was less than 1 year for the majority of late reactions. However, for telangiectasia of the skin and mucous membranes, the LP_{50} was ~ 3.75 years and ~ 1.75 years, respectively. The LP_{50} for atrophy of the mucous membrane was ~ 3 years, but that for atrophy of the skin was < 1 year.

The results of the analysis of the incidence of the different late effects with respect to dose per fraction, number of fractions and overall treatment times are shown in Tables IX–XI, respectively, and the dose–time parameters obtained from these analyses are presented in Table XII. The α/β ratios for any type of late reaction and oedema of the mucous membrane were 3.46 Gy and 5.0 Gy, respectively. An α/β ratio of 10.80 ± 10.37 Gy

Table VII. Reaction-free rates in patients treated with either 3F/wk or 5F/wk radiotherapy in five treatment centers each contributing more than 50 patients; p values refer to the comparisons of the survival from 0 to 5 or 0 to 10 years by the method described by Mantel (1966)

		Centre number											
		11		14		19		21		24		Others	
Type of late reaction	Reaction-free rates at	3F/wk	5F/wk	3F/wk	5F/wk	3F/wk	5F/wk	3F/wk	5F/wk	3F/wk	5F/wk	3F/wk	5F/wk
Any type													
	5 yrs ±SE (%)	46±7	31±6	21±5	21±6	37±10	51±11	32±7	38±7	34±10	32±9	35±6	32±5
		(p = 0.13)		(p = 0.92)		(p = 0.35)		(p = 0.61)		(p = 0.92)		(p = 0.48)	
	10 yrs±SE (%)	40±8	28±6	13±5	21±6	37±10	44±11	32±7	34±8	19±10	25±10	30±6	21±6
		(p = 0.13)		(p = 0.60)		(p = 0.49)		(p = 0.72)		(p = 0.92)		(p = 0.39)	
Skin													
	5 yrs±SE (%)	84±5	83±5	66±6	55±7	93±5	87±7	91±5	91±5	87±7	77±7	76±5	80±4
		(p = 0.73)		(p = 0.33)		(p = 0.50)		(p = 0.63)		(p = 0.31)		(p = 0.65)	
	10 yrs±SE (%)	84±5	77±7	63±7	52±7	87±7	87±7	91±5	90±6	80±10	70±10	70±6	75±5
		(p = 0.57)		(p = 0.32)		(p = 0.81)		(p = 0.92)		(p = 0.33)		(p = 0.71)	
Mucosal													
	5 yrs±SE (%)	53±7	42±7	30±6	33±7	45±10	64±10	39±8	41±8	51±10	46±10	55±6	43±5
		(p = 0.41)		(p = 0.50)		(p = 0.15)		(p = 0.82)		(p = 0.92)		(p = 0.13)	
	10 yrs±SE (%)	47±8	39±7	23±6	31±7	45±10	56±12	39±8	37±8	51±10	34±10	48±7	30±7
		(p = 0.41)		(p = 0.36)		(p = 0.25)		(p = 0.81)		(p = 0.82)		(p = 0.09)	

Table VIII. Time distribution of the number of late radiation reactions in normal tissues after radiotherapy

	Number of cases in relation to the time of appearance of reaction Time from the start of treatment (years)											
Reaction	0.25–1	1–2	2–3	3–4	4–5	5–6	6–7	7–8	8–9	9–10	Total number	Percentage of total cases
Skin												
Any type	89	14	5	7	6	5	4	2	0	1	133	19
Telangiectasia	5	2	3	3	4	2	2	2	0	2	25	4
Fibrosis and atrophy	40	9	2	4	2	3	2	1	0	1	64	9
Oedema	3	0	0	0	0	0	0	0	0	0	3	0.4
Dyspigmentation	53	8	1	2	0	2	2	0	0	0	68	10
Mucous membrane												
Any type	282	28	17	9	6	5	5	2	2	2	358	50
Telangiectasia	49	24	21	11	8	3	4	3	2	2	127	18
Atrophy	11	7	2	6	5	4	3	1	1	1	41	6
Oedema	234	11	7	3	0	1	1	1	1	0	259	36
Others												
Perichondritis	19	0	1	0	0	0	0	0	0	1	21	3
Probable myelitis	2	1	0	0	0	0	0	0	0	0	3	0.4
Dysphagia	73	11	3	2	0	1	0	1	2	0	93	13
Any type of late reaction	354	27	16	11	8	6	5	1	3	2	433	61

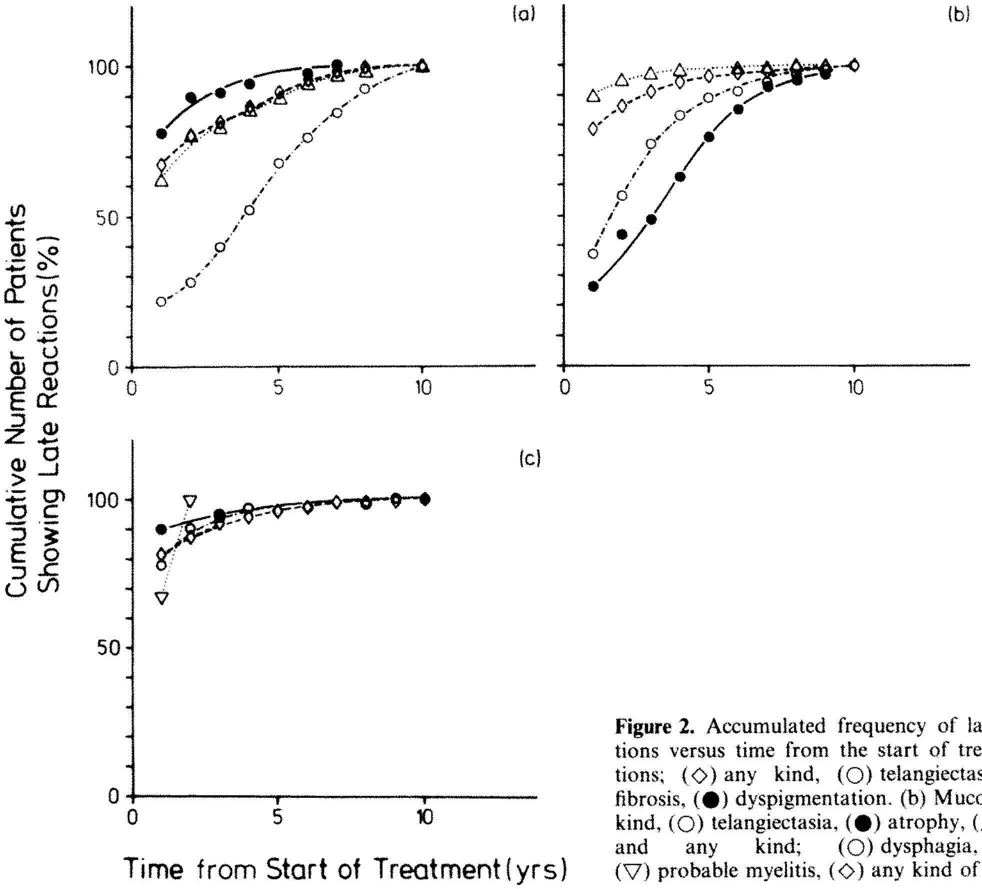

Figure 2. Accumulated frequency of late normal-tissue reactions versus time from the start of treatment. (a) Skin reactions; (◇) any kind, (○) telangiectasia, (△) atrophy and fibrosis, (●) dyspigmentation. (b) Mucosal reactions; (◇) any kind, (○) telangiectasia, (●) atrophy, (△) oedema. (c) Others and any kind; (○) dysphagia, (●) perichondritis, (▽) probable myelitis, (◇) any kind of late effect.

Table IX. Variation in ED_{50} ($\pm$SE) values with dose per fraction for different late normal-tissue reactions. ED_{50} values refer to the maximum tumour dose (Gy)

	Type of normal-tissue reaction		
Dose per fraction (Gy)	Any type of late reaction	Any type of mucous membrane reaction	Oedema of the mucous membrane
2.0	59.45 ± 2.82†	62.19 ± 2.71	66.38 ± 2.45
2.2	63.30 ± 2.35	—	66.73 ± 2.30
2.4	53.10 ± 4.20	57.78 ± 2.85	63.97 ± 2.46
2.6	53.02 ± 2.65	50.12 ± 3.87	59.56 ± 2.96
2.8	55.39 ± 4.02	—	67.56 ± 5.43
3.0	—	—	55.61 ± 2.38
3.2	—	61.19 ± 3.16	62.79 ± 2.96
3.4	—	47.86 ± 5.71	—
3.6	47.37 ± 5.11	—	58.84 ± 2.58
3.9	—	52.92 ± 5.32	49.93 ± 3.43

— No data or insufficient data available.

† 20–68 patients were involved in estimation of each ED_{50} value.

Table X. Variation in ED_{50} ($\pm$SE) values with fraction number for different late normal-tissue reactions. ED_{50} values refer to the maximum tumour dose (Gy)

	Type of normal-tissue reaction		
Number of fractions	Any type of late reaction	Any type of mucous membrane reaction	Oedema of the mucous membrane
12	54.07 ± 2.52†	55.64 ± 3.19	61.68 ± 5.60
13	50.66 ± 3.04	50.41 ± 3.60	52.23 ± 4.44
15	51.20 ± 1.84	—	52.75 ± 3.61
18	50.89 ± 2.12	60.37 ± 1.59	61.82 ± 3.07
19	—	60.47 ± 2.28	—
20	53.97 ± 2.49	—	61.64 ± 4.12
21	50.37 ± 2.51	63.08 ± 1.61	61.26 ± 4.63
25	—	—	64.75 ± 3.26
30	—	—	70.62 ± 3.49
33	—	—	66.15 ± 4.43

— No data or insufficient data available.

† 20–68 patients were involved in estimation of each ED_{50} value.

was obtained for the any type of mucous membrane reaction, but this was not significantly different from zero. There was no correlation between the number of fractions and the ED_{50} values for any kind of late reactions; however, values for the N-exponent of 0.31 ± 0.1 and 0.22 ± 0.07 were obtained for any type of mucous membrane reaction and oedema of mucous membrane, respectively. No time correction was applied in the determination of the α/β ratios and the N-exponents, as no correlation was found between the overall treatment time and the ED_{50} values for these various late normal-tissue reactions.

Discussion

Acute reactions

Almost all patients treated showed some type of acute reaction. However, in more than 50% of these cases, the individual reaction subsided within 4 weeks. The occurrence of different types of reaction may have contributed to the group of patients with any type of acute reaction lasting for $\geqslant$ 4 weeks, *i.e.* 84% of patients. The lack of correlation between these early reactions lasting $\geqslant$ 4 weeks and fraction size, fraction number and overall treatment time could have been caused by the heterogeneity of these end-points. Furthermore, the duration of a lesion might not be solely determined by the radiation dose. There was no difference in the incidence of the early normal-tissue reactions between patients treated with 3F/wk and 5F/wk.

For end-points such as the incidence of ulceration, fibrinous reaction and oedema of the mucous membranes, the time factor was not significantly different from zero. For acute reactions of the skin and for dysphagia, the time factor obtained was consider-

Table XI. Variation in ED_{50} (±SE) values with overall treatment time for different late normal-tissue reactions. ED_{50} values refer to the maximum tumour dose (Gy)

Overall treatment time (days)	Type of normal-tissue reaction: Any type of late reaction	Any type of mucous membrane reaction	Oedema of the mucous membrane
28	51.71±3.07†	—	63.92±5.57
30	57.63±7.59	—	59.63±8.78
32	50.13±7.47†	60.07±6.62	72.07±11.0
33	43.06±6.82	46.81±4.89	50.43±4.83
34	57.48±4.96	64.74±4.83	75.27±9.38
35	54.91±5.18	—	65.70±6.08
37	—	57.70±3.33	—
38	49.38±6.87	—	65.00±7.37
39	54.81±3.78	55.24±2.96	63.53±3.42
40	58.00±6.63	56.20±4.63	63.98±6.53
41	54.79±6.46	52.23±5.54	67.09±6.46
42	55.64±4.70	61.85±3.63	72.14±6.48
43	68.97±7.45	—	—
44	—	58.18±4.53	61.68±4.88
45	49.90±13.07	—	—

— No data or insufficient data available.
† 20–68 patients were involved in estimation of each ED_{50} value.

ably larger than the value of 0.11 associated with the nominal standard dose (NSD) formula. The reverse was true for the *N*-exponent; for dysphagia the *N*-exponent was not significantly different from zero, and for skin reactions the distribution of the responders with regard to total dose in each fixed fraction number group was so poor that no significant dose–effect relationships could be found. Mucosal reactions showed a degree of dependency on the number of fractions, yielding *N*-exponents that were significantly different from zero.

The α/β ratios obtained for the various acute normal-tissue reactions were not significantly different from zero, with the exception of dysphagia. However, the value of α/β of 3.67 Gy obtained for this effect was rather low in comparison with the conventionally accepted values for acutely responding tissues (Fowler, 1984). The value might have been contaminated with the effect of overall treatment time. A lower than conventional value of 4 Gy has also been reported for acute skin reactions in human skin (Trott, 1986).

Table XII. Dose–time parameters for different late normal-tissue reactions. These values were obtained on the basis of the maximum tumour dose

Reaction	α/β (Gy)	*N*-exponent†	*T*-exponent
Any type of late reaction	3.46±1.23*	−0.03±0.06	0.23±0.78
Any type of mucous membrane reaction	10.80±10.37	0.31±0.10*	0.07±0.32
Oedema of mucous membrane	5.0±2.7*	0.22±0.07*	0.12±0.23

† Uncorrected for the effects of overall treatment time.
* Significantly different from zero ($p < 0.05$).

The dose–time parameters obtained for the different types of acute reaction were not conclusive. This might suggest that the reactions have to be recorded very strictly and more frequently until these have subsided.

Late reactions

There was no significant difference in the reaction-free rates for late reactions in patients treated with 3F/wk or 5F/wk analysed collectively or separately for each of the five centres contributing more than 50 patients. Over 60% of all patients showed some type of late normal-tissue reaction.

The time exponents (*T*) for late normal-tissue reactions obtained in the present study were not significantly different from zero. Late oedema of the mucous membrane showed some dependency on the number of fractions, and when combined with other mucous membrane reactions, this dependency was even more apparent. On the other hand, when all late reactions were combined, no dependency on the number of fractions was found. The α/β ratios obtained for any type of late reaction and oedema of mucous membranes of 3.46 Gy and 5.0 Gy were within the range of the α/β ratios usually quoted for late reactions (Fowler, 1984; Thames et al, 1989).

An NSD value of 10 Gy and an *N*-exponent of 0.4

have previously been reported for skin telangiectasia after electron beam therapy (Cohen & Ubaldi, 1977). In the present study, a low (4%) incidence of skin telangiectasia was found and was insufficient to allow any detailed quantitative analysis. This low incidence was probably caused by the skin sparing provided by high-energy photon irradiation. On the other hand, telangiectasia of the mucous membrane developed in 18% of patients but was a less reliable end-point; it requires an indirect examination of the larynx. Telangiectasia of skin and mucous membrane has been attributed to either the cellular depletion and consequent regeneration of the underlying endothelial layer of the vasculature (Cohen & Ubaldi, 1977) or to the degeneration of smooth muscle cells in the walls of arterioles (Hopewell et al, 1989). The progression of these late vascular changes has been estimated by assessing telangiectasia in human skin (Turesson, 1990).

Whatever the underlying mechanisms, telangiectasia of both the skin and mucous membrane was persistent and in some cases it was first reported as late as 10 years after the start of irradiation. It was evident from this study that the incidence of late normal-tissue damage increased progressively with time. This is in agreement with the findings of Turesson (1990), who found that telangiectasia of the skin was progressive for up to at least 10 years. The incidence of late reactions, occurring several years after irradiation, has been reported by Woodhouse et al (1981). These authors reported the development of severe laryngeal oedema 3 years after irradiation, in the 1% of cases that were disease-free. Kogelnik et al (1975) reported the development of severe late radiation effects between 5 and 10 years after radiotherapy for head and neck tumours. Fibrosis of skin was also found to be progressive for periods of longer than 10 years after radiotherapy for breast cancer (Spanos et al, 1980).

The accumulated incidence of telangiectasia of the skin and mucous membranes at 1 year after treatment and the slopes of the frequency curves for these two end-points showed that telangiectasia of the mucous membranes developed faster than telangiectasia of the skin. It was maintained at this faster rate. This might be due to the accumulation of a significantly higher dose in mucous membrane than in skin. The latent period, containing both the frequency and the degree of severity of telangiectasia, has been reported (Turesson & Notter, 1986) to be correlated to radiation dose. Also the short latency period for telangiectasia of mucous membranes could be related to a higher (15%) incidence of acute reactions in mucous membranes. This may have resulted in consequential late effects appearing relatively early. The reverse was observed in the case of atrophy. The rate of development of atrophy after the first year was similar in both skin and mucous membranes; however, within the first year, skin atrophy accumulated considerably faster than that in the mucous membranes. However, it must be recognized that in general it is much easier to observe skin atrophy than atrophy of the mucous membrane. Atrophy of the mucous membrane can be masked by oedema, which is usually more pronounced and more durable in the mucous membrane than in skin.

A better understanding of the time-related distribution of late normal-tissue reactions is an important aid in the design of clinical trials involving radiotherapy. Awareness of the relatively early incidence of late normal-tissue reactions would certainly prevent unnecessary prolongation of follow-up of patients. Over 80% of the normal-tissue reactions seen were observed within the first year after the start of the treatment, and 96% were observed in the first 5 years. This implies that follow-up periods beyond 5 years did not contribute significantly to the reliability of the conclusions drawn from the trial with respect to the incidence of late effects (Haybittle et al, 1990). However, among the end-points investigated, the incidence of telangiectasia of the skin and mucous membranes and atrophy of mucous membranes increased more slowly than the other late effects. Shortening of the follow-up period to 5 years will obviously underestimate the number of patients showing these specific reactions. This would be most pronounced in the case of telangiectasia of the skin, which was the slowest developing lesion. Turesson (1990) demonstrated that the rate of progression of the skin telangiectasia was both dose- and time-dependent. She demonstrated a considerable reduction in the value of the isoeffective dose with increasing time of follow-up until the 9th year (the final assessment time). The decrease in ED_{50} values was associated with a significant increase in the steepness of the dose–response curves until 5 years. No changes were seen between 5 and 9 years.

The α/β ratio of 3.46 ± 1.23 Gy for the late effects results in this study corresponds to the value of 3.8 Gy for cartilage necrosis and severe oedema of the larynx after radiotherapy of supraglottic tumours reported by Maciejewski et al (1986). These authors also found no time factor relating to these late complications. On the other hand, Turesson and Thames (1989) have reported a small but significant time factor for telangiectasia of human skin when the overall times varied between 12 and 40 days. The α/β ratio they obtained was 3.9–4.3 Gy, which was comparable to the value of 3.46 Gy obtained, for any kind of late effects, in the present study.

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Lung function and radiation response

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Keywords: Haemoglobin, Respiratory function, Tumour response, Acute morbidity, Radiotherapy

Abstract. This study investigated whether impaired respiratory function affected the response to radiotherapy. A prospective study was performed in which lung function, arterial oxygen and haemoglobin concentration were examined, before treatment with radical radiotherapy, in 141 patients with advanced non-small cell lung cancer and head and neck cancer. The findings were considered to reflect the physiological conditions present at the time of radiotherapy and these were related to acute normal tissue reactions and tumour control. Although 53% of the patients showed some impairment of lung function and 47% demonstrated a haemoglobin oxygen saturation below the normal range, oxygen partial pressure was below expected levels in fewer patients (27%) and total arterial oxygen content was below normal in only 12% of patients. No correlation was found between the tests performed and the severity of acute morbidity or with local tumour control. In the patients with carcinoma of the bronchus, there was a trend for incomplete tumour control to be associated with a lower haemoglobin level, but this did not reach statistical significance. In patients selected for curative radiotherapy, lung function would not appear to be an important factor influencing the response of normal tissues or tumour to irradiation.

There is clinical evidence that anaemia is associated with an impaired outlook in patients treated with radiotherapy at a number of sites (Dische, 1991), including the uterine cervix (Evans & Bergsjø, 1965; Hierlihy et al, 1969; Vigario et al, 1973; Shreiner et al, 1975; Bush et al, 1978; Overgaard et al, 1989), bladder (Quilty & Duncan, 1986), head and neck (Overgaard et al, 1986; Taskinen, 1969), bronchus (Dische et al, 1986 & 1988) and corpus uteri (Rustowski & Kupsc, 1982). Reduced availability of oxygen is believed to lead to tumour hypoxia and so to radioresistance. Therefore, in the preparation of patients for treatment, the correction of anaemia is regarded as important (Dische et al, 1986).

Hypoxia due to reduced saturation of haemoglobin with oxygen may occur as a result of pulmonary dysfunction. Respiratory impairment is a common problem in patients with tumours, especially those where tobacco has been a causative factor. However, little attention has been given to the relationship between pulmonary function and radiation response.

We performed lung function tests and arterial blood gas analysis before radiotherapy in 141 patients with advanced non-small cell carcinoma of the bronchus and squamous cell carcinoma of the head and neck. The findings were related to radiation response in tumour and in normal tissues.

Patients and methods

All patients included in a study of continuous hyperfractionated accelerated radiation therapy (CHART) routinely underwent tests of pulmonary function before treatment (Saunders et al, 1988 & 1989). There were 65 patients with advanced non-small cell carcinoma of the bronchus and 76 with advanced squamous cell carcinoma in the head and neck region who were considered suitable for definitive radiotherapy. They were treated between January 1985 and March 1989 (Table I). Initially, patients received a minimum tumour dose of 50.4 Gy but in May 1986 this was elevated to 54.0 Gy. The treatment was given in 36 fractions, three being given each day with an interfraction interval of 6 h, over a continuous period of 12 days (Saunders et al, 1988 & 1989). Patients were followed up for a minimum of 9 months and were examined closely to determine tumour response and normal tissue effects.

The respiratory function studies performed before treatment are shown in Table II. They are divided into tests of ventilation, measurement of carbon monoxide diffusing capacity and arterial blood studies. From the different ventilatory measurements, patients were grouped into three categories of pulmonary function according to the degree of impairment (Table III). This empirical classification developed by Lockwood (1980) was derived from results obtained by spirometry. In prospective studies it has proved reliable in predicting

Table I. Patient details

	Bronchus	Head and neck
Male	47	54
Female	18	22
Total	65	76
Age range (years)	42–76	23–83
Mean age (years)	64	63

Table II. Lung function tests

Forced ventilation	
	Forced vital capacity (FVC)
	Forced expiratory volume in 1 s (FEV_1)
	$FEV_1\%$
	Maximum voluntary ventilation (MVV) FEV_{40}
	Maximal mid-expiratory flow rate (MMFR)
Flow rates:	Maximal expiratory flow rate (MEFR)
	Flow rates after expiration of 25%, 50%, 75% FVC
	Maximal inspiratory flow rate (MIFR)
Lung volumes:	Total lung capacity (TLC)
	Vital capacity (VC)
	Forced vital capacity (FVC)
	Residual volume (RV) and RV%
	Functional residual capacity (FRC)
Carbon monoxide diffusing capacity	
	Transfer factor (TL_{CO})
	Transfer coefficient (K_{CO})
	Effective lung volume (V_A)
Blood gas studies	
	pH
	pCO_2
	pO_2
	Bicarbonate
	Base excess
	Standard bicarbonate
	% Saturation
	Alveolar – arterial oxygen difference
	Arterial oxygen content

Table III. Method used to classify patients into three categories of pulmonary function based on results of spirometry

If either:

(1) Maximal mid-expiratory flow rate is less than 1.2 l/s

Or:

(2) at least three of the following are outside the limits:

Forced vital capacity is less than 2.56 l
Forced expiratory volume in 1 s is less than 1.64 l
Maximum voluntary ventilation is less than 52 l/min
Residual volume is more than 2.08 l
Total lung capacity is more than 6.13 l
Residual volume/total lung capacity ratio is more than 37.5%

—then patients are considered to have "impaired" lung function. Patients in whom both (1) and (2) are abnormal have "considerable impairment" of lung function.

the risk of post-operative complications in patients with bronchogenic carcinoma undergoing thoracotomy. We adopted this method to give an overall expression of the degree of functional disability. Tumour response and acute morbidity were assessed for each category of pulmonary function.

From the measurement of carbon monoxide diffusing capacity, the transfer factor and the transfer coefficient were determined. The transfer coefficient is a measure of the diffusing capacity, independent of lung volume. This was expressed as a percentage of the expected value for age and sex, and was related to tumour response and to acute effects in normal tissue, independently of the other tests of lung function. Based on clinical experience it was found that levels below 70% of those expected are associated with abnormality, while values from 70% to 100% are of doubtful significance. Therefore, the patients were divided into three groups: those with transfer coefficients of less than 70% of the expected value, those with 70–100% of the expected value and those with levels greater than 100% of the predicted value.

Arterial blood gases and haemoglobin were measured to examine the relationship between percentage saturation of haemoglobin, partial pressure of oxygen (PaO_2), arterial oxygen content and haemoglobin with radiation response. For each parameter, patients were divided into three groups according to the results obtained.

The normal range of oxygen saturation of haemoglobin is between 95% and 99% with a mean of 97.5%. The oxygen carrying capacity of blood falls off rapidly as saturation drops and at levels below 90% the patient becomes symptomatic. Patients were divided into three groups: those with a saturation level below 90%, those with saturation levels between 90% and 95% and those with levels greater than 95%.

The arterial PaO_2 progressively decreases with age. In the age group 60–69 years, 71 mmHg (9.5 kPa) is the lower limit of the normal range and the mean is 81 mmHg (10.8 kPa) (Nunn, 1987). As the mean age was 65 years, these values were used to divide the patients into three groups: those with PaO_2 less than 71 mmHg, those with PaO_2 between 71 and 81 mmHg and those with PaO_2 greater than 81 mmHg.

Oxygen in arterial blood combines mainly with haemaglobin, though some is carried in physical solution in erythrocytes and plasma. The total oxygen available is given by the formula:

$$\text{Oxygen content of blood (ml/dl)} = (0.003 \times PaO_2) + (\text{saturation} \times Hb \times 1.39)$$

where the amount of oxygen carried in blood in solution at 37°C is 0.003/100 ml per mmHg, PaO_2 is the partial pressure of oxygen in arterial blood (mmHg), Hb is the haemoglobin concentration (g/dl) and 1.39 is the volume (ml) of oxygen which theoretically can combine with 1 g of haemoglobin (Nunn, 1987). Arterial oxygen content varies with pH, base excess, temperature and haemoglobin concentration, and tables showing the oxygen content of human blood as a function of these variables have been published (Nunn, 1987). At pH 7.4 and base excess 0, the lower limit of the normal range of oxygen content is 15.7–21.6 ml/dl in women and 17.6–24.3 ml/dl in men. To examine the effect of arterial oxygen content on radiation response, patients were divided into three groups: those with arterial oxygen

Table IV. Results of blood gas analysis

	Bronchus			Head and neck			Normal range
	Range	Median	SD	Range	Median	SD	
Saturation %	88.0–98.2	94.7	1.77	74.7–99.0	94.5	3.89	95.0–99.0
PaO_2 (kPa)	7.8–12.1	10.0	0.94	5.4–13.3	10.3	1.41	9.5–12.1
Arterial oxygen concentration (ml/dl)	13.6–22.5	17.6	2.05	14.7–22.4	18.4	1.54	15.7–24.3
Haemoglobin (g/dl)	10.2–16.7	13.5	1.48	9.1–16.7	13.6	1.33	11.5–18.0

content less than 16 ml/dl, those with values in the range 16–19 ml/dl and those with values greater than 19 ml/dl.

To assess the influence of haemoglobin, patients were arbitrarily divided into three groups: those with haemoglobin concentrations of less than 12.5 g/dl, those between 12.5 and 14.5 g/dl and those with concentrations greater than 14.5 g/dl.

In the patients with head and neck carcinoma tumour regression was assessed clinically. For the patients with carcinoma of the bronchus, tumour response was assessed from serial chest X rays and computed tomography (CT) scans. In both groups the minimum period of follow-up was 9 months after commencement of treatment. As a complete tumour response has the greatest prognostic significance (Dische et al, 1980; Saunders et al, 1984), for this analysis patients were divided into two groups: those who showed a complete response and those with residual or recurrent disease at the time of analysis.

In patients with carcinoma of the head and neck, acute morbidity was measured by the duration or persistence of mucositis. In patients with bronchogenic carcinoma it was measured by the time taken for dysphagia to settle completely (Saunders et al, 1988 & 1989). In addition to analysis in the above subgroups, multivariate analysis of the prognostic variables was performed using the stepwise logistic procedure for tumour response and the Cox model for acute morbidity in the SAS software package.

Results

Table IV shows the range and mean values (±SD) obtained for the percentage saturation of haemoglobin, arterial oxygen tension, arterial oxygen content and haemoglobin levels in the two groups of patients. Median values in both sets of patients fell approximately within the normal range of values.

Table V. Distribution of patients in categories of pulmonary function, according to results of spirometric tests, arterial blood studies and haemoglobin concentration

	Bronchus no. (%)	Head and neck no. (%)
Ventilatory tests		
Considerable impairment	11 (18)	13 (20)
Impairment	26 (42)	17 (27)
Normal	25 (40)	34 (53)
Transfer coefficient		
<70%	7 (12)	16 (27)
70–100%	23 (40)	29 (48)
>100% (normal)	27 (47)	15 (25)
Percentage haemoglobin saturation		
<90%	2 (4)	3 (5)
90–95%	29 (54)	19 (33)
>95% (normal)	23 (42)	36 (62)
Oxygen partial pressure		
<9.5 kPa	18 (33)	12 (21)
9.5–10.8 kPa } (normal)	30 (56)	29 (50)
>10.8 kPa } (normal)	6 (11)	17 (29)
Arterial oxygen content		
<16 ml/dl	9 (17)	4 (7)
16–19 ml/dl } (normal)	28 (52)	34 (59)
<19 ml/dl } (normal)	17 (31)	20 (34)
Haemoglobin		
<12.5 g/dl	18 (28)	14 (18)
12.5–14.5 g/dl	29 (45)	42 (55)
>14.5 g/dl	18 (28)	20 (26)

Tests of ventilation and transfer coefficient

Ventilatory tests of lung function were performed in 62 of the 65 patients with bronchial carcinoma and in 64 of the 76 patients with head and neck cancer. The distribution of patients within the three categories of pulmonary function is shown in Table V. Some impairment of lung function was seen in 37 (60%) patients with bronchial carcinoma and in 30 (47%) patients with head and neck carcinoma. Tumour control in each group is shown in Table VI. No difference between the groups was observed.

The transfer coefficient was detmined in 57 of the 65 patients with carcinoma of the bronchus and in 60 of the 76 patients with head and neck carcinoma. In seven (12%) of those with bronchial carcinoma and 16 (27%) with head and neck carcinoma, there was some impairment of diffusing capacity, the transfer coefficient being less than the lower limit of the expected value (Table V). Table VI shows that there was no difference in tumour response according to the transfer coefficient. With respect to the acute normal tissue reaction, no correlation with ventilatory assessment or with the transfer coefficient was observed.

Arterial blood studies

Percentage saturation of haemoglobin. The percentage of haemoglobin saturation was measured in 54 patients with bronchial carcinoma, and in 31 (57%) cases the levels were less than 95%. In 22 of the 58 (38%) patients with head and neck carcinoma, the saturation was below 95% (Table V). No difference in tumour control was seen (Table VI), nor was there any difference in the duration of dysphagia or mucositis.

Arterial PaO_2. The arterial oxygen tension was determined in 54 of the 65 patients with bronchogenic carcinoma and in 58 of the 76 patients with head and neck carcinoma. PaO_2 was below the lower limit of the normal range in 18 (33%) patients with carcinoma of the bronchus and in 12 (21%) patients with head and neck carcinoma (Table V). Tumour response for each of the three groups is shown in Table VI. There was no correlation between arterial oxygen partial pressure and tumour control or acute normal tissue morbidity.

Arterial oxygen content. The arterial oxygen content was determined in 54 of the 65 patients with bronchial carcinoma and in nine (17%) cases this was less than 16 g/dl. In only four (7%) of the 58 patients with head and neck carcinoma was the arterial oxygen content less than 16 g/dl (Table V). Table VI shows tumour response according to arterial oxygen content. No difference in tumour response or acute normal tissue morbidity was observed.

Haemoglobin level

Before the commencement of radiotherapy, haemoglobin concentration was determined in all patients (Table V) and the relationship between this and tumour control is shown in Table VI. The haemoglobin concentration was less than 12.5 g/dl in 18 of the 65 patients with bronchial carcinoma and, in this group, 17%

Table VI. Tumour control in each category of pulmonary function

	Bronchus total no. (%)		Head and neck total no. (%)	
	No.	CR	No.	CR
Ventilatory tests				
Considerable impairment	11	5 (45)	13	10 (77)
Impairment	26	6 (23)	17	12 (71)
Normal	25	7 (28)	34	20 (59)
Transfer coefficient				
<70%	7	1 (14)	16	11 (69)
70–100%	23	7 (30)	29	20 (69)
>100%	27	9 (33)	15	8 (53)
Percentage haemoglobin saturation				
<90%	2	0 (0)	3	1 (33)
90–95%	29	8 (28)	19	10 (53)
>95%	23	7 (30)	36	22 (61)
Oxygen partial pressure				
<9.5 kPa	18	5 (28)	12	7 (58)
9.5–10.8 kPa	30	9 (30)	29	19 (66)
>10.8 kPa	6	1 (17)	17	11 (65)
Arterial oxygen content				
<16 ml/dl	9	2 (22)	4	2 (50)
16–19 ml/dl	28	6 (21)	34	22 (65)
>19 ml/dl	17	7 (41)	20	13 (65)
Haemoglobin				
<12.5 g/dl	18	3 (17)	14	11 (79)
12.5–14.5 g/dl	29	8 (28)	42	24 (57)
>14.5 g/dl	18	7 (39)	20	12 (60)

showed and maintained a complete response, compared with 39% of the 18 patients with haemoglobin levels greater than 14.5 g/dl. The trend for an association between haemoglobin concentration and tumour control did not reach statistical significance ($p < 0.25$, χ^2 test). In the patients with head and neck cancer, there was no difference in tumour control between the groups divided according to haemoglobin concentration. In order to overcome the complicating factor of differing normal ranges of haemoglobin concentrations in males and females, analyses were performed in which all levels in females were elevated by 1 g. However, this did not alter the results obtained. No effect on acute normal tissue morbidity was observed.

To determine which lung function variables had significant independent prognostic value, in terms of acute normal tissue morbidity and complete tumour regression without recurrence, a multivariate analysis was carried out. All the covariates listed in Table II were entered into the model and the significance level for entry was $p < 0.3$. None appeared to be an independent prognostic indicator at the level $p < 0.05$.

Discussion

In the patients studied some respiratory impairment can be expected, either as a result of chronic lung disease induced or exacerbated by smoking, or as a result of the presence of the carcinoma. Therefore, many patients would be expected to demonstrate poor ventilation and, in some cases, hypoxia due to impaired saturation of haemoglobin.

Using Lockwood's overall assessment of the results of the ventilation tests, 60% of the patients with bronchial carcinoma and 47% of those with head and neck carcinoma did have impairment of lung function. When lung function was assessed by carbon monoxide diffusion, 12% of patients with carcinoma of the bronchus and 27% of those with head and neck carcinoma had levels less than the lower limit of the predicted value for age and sex. However, it should be noted that where a portion of the lung is perfused but not ventilated, as in bronchial carcinoma, compensatory processes may occur in the remaining lung, which will result in a higher transfer coefficient.

Impairment of haemoglobin saturation below 95% was found in 57% of patients with bronchial carcinoma and in 38% of patients with carcinoma in the head and neck region. However, the impairment was minor, in most cases lying in the range of 90–95%. Only two patients with bronchial carcinoma and three with head and neck carcinoma showed arterial oxygen saturations below 90%.

When hypoxaemia was investigated there were fewer abnormal values. Arterial PaO_2 levels were below the normal range in 33% of patients with bronchial carcinoma and in 21% of those with head and neck carcinoma. Arterial oxygen content was below normal limits in 17% of patients with bronchial carcinoma and in 7% of those with head and neck carcinoma.

Despite the abnormalities revealed, no relationship could be demonstrated between lung function and radiation response, either acutely in the normal tissues or with tumour control.

A review of the literature has revealed only two studies which relate to this present study. In a murine model, Siemann et al (1975) reported an increase in tumour growth delay after radiotherapy as arterial PaO_2 increased. Sasai et al (1989) published the results of the only clinical study, giving figures for 42 patients with epidermoid bronchogenic carcinoma treated by radiotherapy alone, correlating arterial oxygen content, arterial oxygen partial pressure and haemoglobin concentrations with the extent of tumour regression and survival. There was a statistically significant correlation between all three factors with the extent of regression of the primary tumour after radiotherapy; arterial oxygen content showed the strongest association. Patients with haemoglobin levels greater than 11 g/dl and arterial oxygen partial pressure greater than 90 mmHg (12 kPa) showed significantly longer survival, but an arterial oxygen content greater than 14.5 ml/dl was the most important factor correlating with survival. It was concluded that arterial oxygen content was a more important prognostic factor than haemoglobin level.

The present study demonstrated no relationship between arterial oxygen content and tumour response, and the patients with bronchogenic carcinoma differed greatly from those reported by Sasai et al (1989). 21 of the 42 (50%) patients included in that study had haemoglobin levels of less than 11 g/dl and in six patients the haemoglobin was less than 9 g/dl. In this study, only three of the 65 patients had haemoglobin levels of less than 11 g/dl. It is unusual in our practice to treat radically under the conditions described by Sasai et al (1989). For CHART, female patients with haemoglobin levels below 11.5 g/dl and males with levels less than 12.5 g/dl were transfused before radiotherapy, but this was indicated in less than 5% of the cases selected for treatment. In 11 of the 42 patients reported by Sasai and his colleagues, the arterial oxygen content was less than 14.5 ml/dl, whereas only two in our group had an arterial oxygen content less than 14.5 ml/dl.

Examination of the formula for calculating oxygen concentration in the blood shows that the haemoglobin concentration is by far the most important factor dominating the value obtained. However, this present study did not show a statistically significant correlation between haemoglobin concentration and the radiation response of normal tissues and tumour in either group. In patients with bronchial carcinoma there was a trend for less tumour control in those with lower haemoglobin, but with the total of 62 cases this did not reach statistical significance. In a previous study of carcinoma of the bronchus, a survival advantage in patients with haemoglobin levels above 13.5 g/dl was found (Dische et al, 1986).

Overgaard et al (1986) showed that in a subgroup of male patients with carcinoma of the supraglottic larynx and pharynx, anaemia influenced tumour control when a haemoglobin level of 14.5 g/dl was used to divide the cases. Among the patients with head and neck cancer in the present study, there were only 21 male patients with such tumours. Tumour control rates were similar at 67% in the nine patients with haemoglobin levels above 14.5 g/dl as in the 12 with lower levels. For our group overall, as with other head and neck sites reported by Overgaard et al (1986), haemoglobin did not influence tumour control.

Conclusions

Impaired respiratory function is common in patients with carcinoma of the bronchus and in the head and neck region. In some, as a result, there is a degree of impairment of saturation of haemoglobin and hypoxaemia. However, in the analysis of all the tests of lung function, no relationship with acute normal tissue reaction or tumour control has been shown. The respiratory reserve of the majority of these patients is impaired, but at rest, the conditions under which radiotherapy is given, patients selected and prepared for curative treatment show only mild changes in arterial oxygen content which do not appear important in moderating radiation response.

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Time-related changes in lymphatic clearance in pig skin after a single dose of 18 Gy of X rays

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Abstract. The early and late effects of X rays on lymphatic microcirculatory function have been investigated in pig skin. Paired estimates of lymph clearance were performed in irradiated and unirradiated sites on the flank skin of anaesthetized Large White pigs at 3, 6, 9, 12, 26, 39, 52, 64 and 78 weeks after a single dose of 18 Gy of X rays. The dermal clearance of ^{99}Tc^{m}-colloid was used to assess lymph flow. The results demonstrated two waves of impaired lymphatic clearance which correlated well with the gross morphological changes observed. The first wave occurred between 6 and 12 weeks after irradiation and corresponded to a period of ischaemia and oedema. The second wave, at 52 weeks, corresponded with dermal thinning and subcutaneous atrophy. X irradiation resulted in an impairment of lymph drainage both within and outside the field of irradiation. Impaired lymphatic drainage probably contributes to the gross and histological changes observed in the skin after X irradiation.

All radiotherapy procedures by necessity involve the irradiation of the skin. In particular, injury to the skin limits the dose of radiation which can be delivered safely to deeply situated tumours. Gross and histological changes in human skin after irradiation have suggested that damage to the vascular system plays an important role in the pathogenesis of late damage (Rubin & Casarett, 1968; Tessmer, 1971). Studies in pig skin correlating functional and morphological changes in blood vessels after irradiation have supported the human experience (Archambeau et al, 1984; Hopewell, 1990). Vascular damage consistent with an 80% reduction in dermal blood flow, 12 weeks after irradiation, resulted in ischaemic necrosis in 50% of irradiated skin areas after a single dose of 20.7 Gy (Moustafa & Hopewell, 1979; Young & Hopewell, 1982) and corresponded with a histological reduction in vascular density. Focal occlusive changes in arterioles, particularly in the deep dermis, were prominent and small thrombi were seen (Hopewell, 1980). Therefore, necrosis would appear to develop as a result of vascular insufficiency. Dermal oedema is also pronounced between 9 and 12 weeks and this progresses to atrophy of the reticular dermis and subcutaneous fat as late radiation damage ensues (Baker et al, 1989).

The lymphatics, in partnership with blood vessels, work in controlling the environment of every cell in the body (homeostasis). Their purpose is to drain from the tissues all macromolecules, cellular waste products, organic and inorganic material which cannot exit directly via the blood stream. In addition they play an important role in preventing oedema (Mortimer, 1990).

Little or no attention has been given to the lymphatics when considering radiation-induced effects on normal tissues. Qualitative changes in lymphatic vessels have not been described, presumably because of the difficulties associated with their identification in histopathological sections. Oedema and connective tissue changes are well known sequelae of lymphatic damage (Altorfer & Clodius, 1976). Therefore, lymph flow studies were undertaken in pig skin in order to investigate if lymphatic insufficiency contributes to the development of late effects in the skin following X irradiation.

The skin of the young female Large White pig was chosen for these studies because it exhibits considerable structural similarity to that of man (Montagna & Yun, 1964). In addition, the effects of ionizing radiation are comparable in pig skin with that of man, both in terms of gross macroscopic changes as well as for morphological and functional parameters.

The isotope clearance technique used for the measurement of lymphatic function has been shown to be consistent and reliable when performed as a group test, under controlled laboratory conditions, in the normal flank skin of the Large White pig (Mortimer et al, 1990). The technique can identify circumstances in which lymphatic impairment exists.

Materials and methods

Animals. Two female pigs of the English Large White strain were used in these investigations. The animals were admitted to the animal house at 10–12 weeks of

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age and allowed to acclimatize for 2 weeks before any investigations commenced. All investigations were carried out under anaesthesia maintained with 2% halothane in a mixture of ~ 30% nitrous oxide and ~ 70% oxygen (Dickinson & Hubbard, 1990). Ambient temperature for these studies was maintained between 20 and 24°C. Irradiation studies were commenced when the animals were 19 weeks old.

Irradiation. 1 week before irradiation 6 standard fields measuring 4 cm × 4 cm were tattooed with india ink on the left flank of each pig. Fields were separated from each other by 8 cm. At the time of irradiation those skin fields were further delineated by a Perspex-ended applicator and a 4 cm × 4 cm cut-out in 3 mm lead placed on the skin surface. A single dose of 18 Gy was given to each skin field at a dose-rate of 0.68 Gy/min from a 250 kV X-ray unit operating at 15 mA with 0.5 mm Cu and 1.0 mm Al added filtration (half-value layer (HVL) 1.4 mm Cu).

Lymphatic clearance. The rate of removal of an intradermally injected radiolabelled colloid, cleared exclusively by lymph vessels, provides an index of lymphatic function in the skin (Fernandez et al, 1983). Full details of the method developed to assess lymph flow in pig skin have been described previously (Mortimer et al, 1990).

Measurements of lymph flow by isotope tracer clearance, were performed simultaneously in irradiated and "control" unirradiated skin, between irradiated fields, after the superficial intradermal injection of ^{99}Tc^{m}-rhenium sulphide colloid (Lymphocis, CIS, UK). The clearance was monitored using two matched collimated NaI crystal scintillation detectors positioned over the injection sites, with the collimator surfaces 10 mm from the skin. The detectors were connected to a multichannel analyser (Nuclear Data Inc. ND62), operating in the multiscaler mode, to provide a digital output of radioactive counts with time (10 s counting intervals). A total recording time of 30 min was used. Up to 12 comparative paired lymph flow determinations, a maximum of six on each animal, were performed at intervals of 3, 6, 9, 12, 26, 39, 52, 64 and 78 weeks after irradiation.

Data analysis. Changes in radioactive counts were plotted as the percentage of the maximum count-rate against time. The resulting clearance curves were analysed using a single exponential equation as described previously (Mortimer et al, 1990). The data points were fitted to this equation using a non-linear least square method based on Marquardt (1963). The clearance results were corrected for the decay of ^{99}Tc^{m} ($t_{\frac{1}{2}} = 6$ h) and lymph flow was expressed as a half clearance time ($t_{\frac{1}{2}}$) in hours.

Results

Macroscopic observations of irradiated skin sites, at the time of each functional assessment, detected moderate to bright red erythema after 3–6 weeks, mauve/dusky erythema with clinically evident oedema after 9–12 weeks and subcutaneous induration at later times. Clearance curves obtained from unirradiated skin sites consistently showed a steep initial gradient, while in irradiated fields there was a comparative delay in the clearance of the tracer. This steep initial slope in the clearance of the tracer from the unirradiated fields was not large enough to influence the overall shape of the

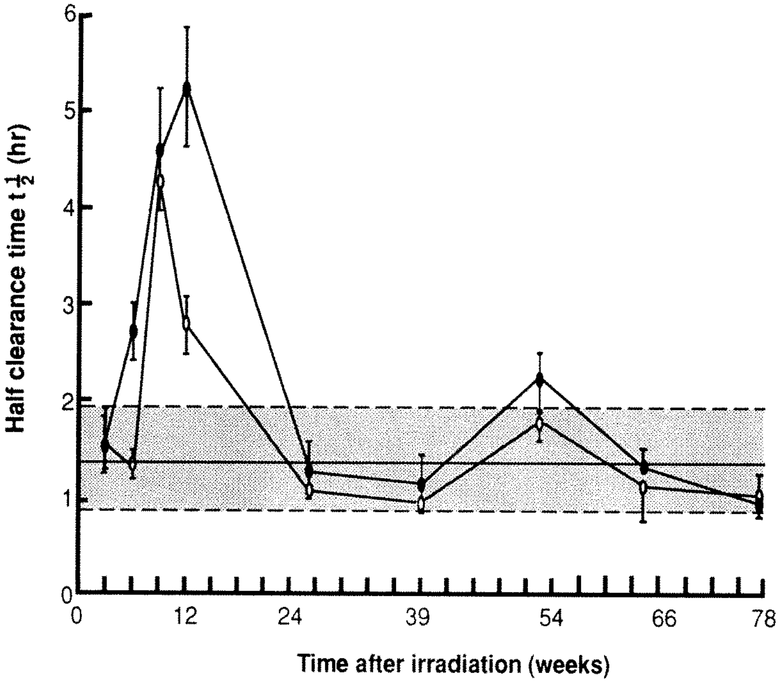

Figure 1. Time-related changes in the clearance of ^{99}Tc^{m}-colloid from the dermis of the flank of the pig following irradiation with a dose of 18 Gy of X rays. Results are expressed as the mean half clearance times (±SE) for irradiated (●) and non-irradiated (○) fields. The shaded area represents the mean $t_{\frac{1}{2}}$ value (±SE) in normal skin. Error bars indicated.

clearance curve. The clearance of the tracer *versus* time, after injection in both irradiated and unirradiated skin fields, was adequately described by a monoexponential equation.

The time-related changes in lymphatic clearance from pig skin following a single dose of 18 Gy are shown in Figure 1. Two waves of radiation induced change were observed. The first wave occurred between 6 and 12 weeks after irradiation. The second wave of impaired lymphatic clearance occurred at 52 weeks.

Surprisingly, these two waves of impaired lymphatic clearance were also observed in the non-irradiated "control" sites between the irradiated fields. Therefore, the mean clearance rate measured in the same two pigs and in the same flank, but before irradiation, was used as representing normal clearance ($t_{\frac{1}{2}} \pm$ standard error (SE) $= 1.4 \pm 0.12$ h) (Mortimer et al, 1990). No significant change in the half clearance times was seen at 3, 6, 26, 39, 64 and 78 weeks. From the sequence of changes with time there would appear to be a substantial impairment of $^{99}\mathrm{Tc}^{m}$-colloid clearance in unirradiated fields at 9 and 12 weeks and again possibly at 52 weeks. No alteration in the appearance of the skin was observed at these unirradiated sites.

At 6 weeks after X irradiation, the mean value of the half clearance time ($\pm$SE) for irradiated fields was 2.81 ± 0.36 h compared with 1.32 ± 0.08 h for unirradiated fields. The difference was significant ($p < 0.001$).

At 9 weeks after X irradiation, no significant differences were detected in clearance times between irradiated and unirradiated sites, with both $t_{\frac{1}{2}}$ values being prolonged. The mean $t_{\frac{1}{2}}$ ($\pm$SE) for irradiated fields was 4.75 ± 0.81 h compared with 4.39 ± 0.31 h for unirradiated fields (Fig. 2).

At 12 weeks a significant difference was observed in the paired lymphatic clearance measurements for irradiated and unirradiated skin. The mean $t_{\frac{1}{2}}$ value ($\pm$SE) for irradiated fields was 5.26 ± 0.66 h and for unirradiated fields it was 2.90 ± 0.33 h ($p < 0.02$) (Fig. 3). Clearance values returned to normal in both irradiated and unirradiated fields at 26 and 39 weeks after irradiation (Fig. 3).

At 52 weeks post-irradiation clearance was again slow compared with normal in both irradiated ($p < 0.001$) and unirradiated ($p < 0.01$) fields, but significantly more in the areas receiving X rays ($p < 0.05$). The mean $t_{\frac{1}{2}}$ value ($\pm$SE) for irradiated fields was 2.46 ± 0.2 h and for unirradiated fields 1.96 ± 0.09 h (Fig. 4).

At 64 and 78 weeks after X irradiation mean $t_{\frac{1}{2}}$ values returned to normal in both irradiated and unirradiated sites. When the variation in the response of each individual animal used in the study was examined, it was found that there was no statistical difference between the two pigs (Table I).

Discussion

Gross morphological changes in the skin following irradiation with a single dose of X rays have been well documented in the pig (Hopewell, 1986 and 1990). Two distinct waves of radiation-induced damage have been observed. The first relates to a vasodilation of the dermal blood vessels and corresponds to an increase in skin blood flow at 3 weeks (Moustafa & Hopewell, 1979; Young & Hopewell, 1982). The second wave, characterized by a mauve/dusky erythema at 12 weeks, represents dermal ischaemia which has been confirmed by the measurement of reduced isotope ($^{99}\mathrm{Tc}^{m}$) clearance. This ischaemia is associated weith oedema and

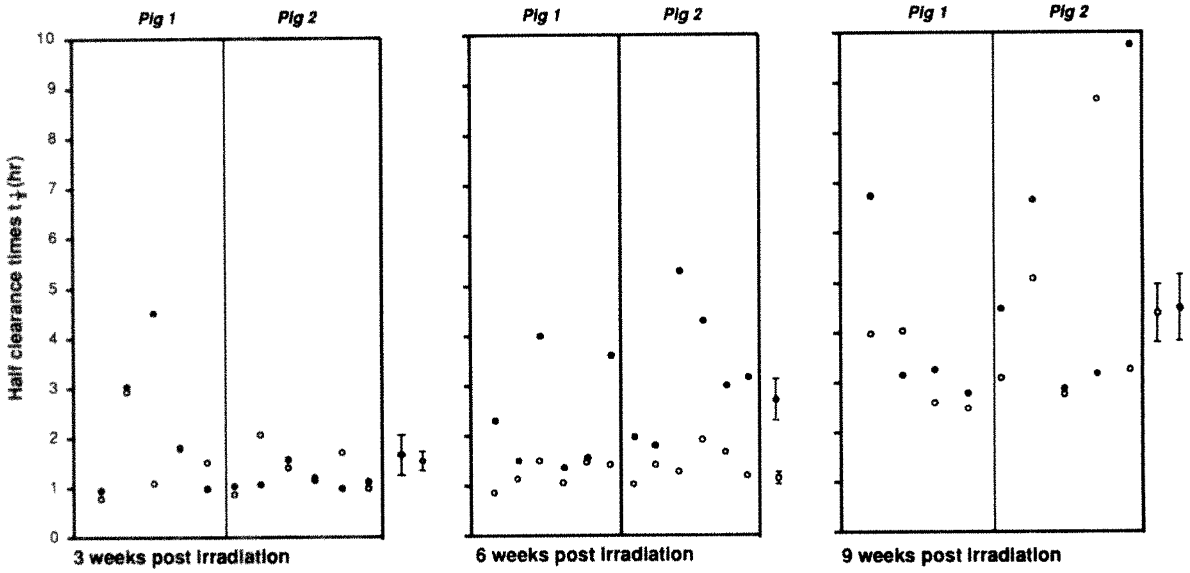

Figure 2. Individual and mean half clearance times ($t_{\frac{1}{2}}$ h) of each lymph clearance determined in irradiated (●) and non-irradiated (○) skin at intervals of 3, 6 and 9 weeks after a single dose of 18 Gy of X rays.

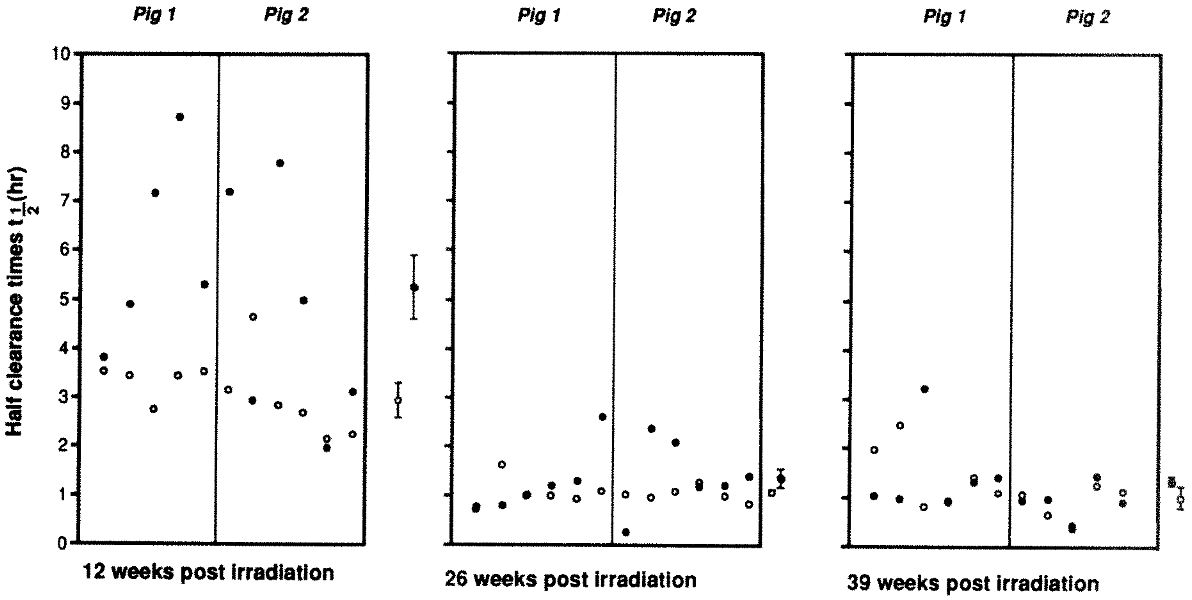

Figure 3. Individual and mean half clearance times ($t_{\frac{1}{2}}$ h) of each lymph clearance determined in irradiated (●) and non-irradiated (○) skin at intervals of 12, 26 and 39 weeks after single dose of 18 Gy of X rays.

histologically with occlusive vascular changes and subsequently a reduced vascular density (Hopewell, 1980). Between 12 and 104 weeks, when late tissue damage develops, blood flow measurements return to and remain normal, probably because of the atrophy of parenchymal tissues which returns the blood vessel density to normal.

In the present study, the early and late effects of X irradiation on lymphatic microcirculatory function have been investigated in pig skin. The two waves of impaired lymphatic clearance observed correlate with the gross morphological changes. The first wave occurred between 9 and 12 weeks after irradiation and corresponded to the period of ischaemia and oedema. The

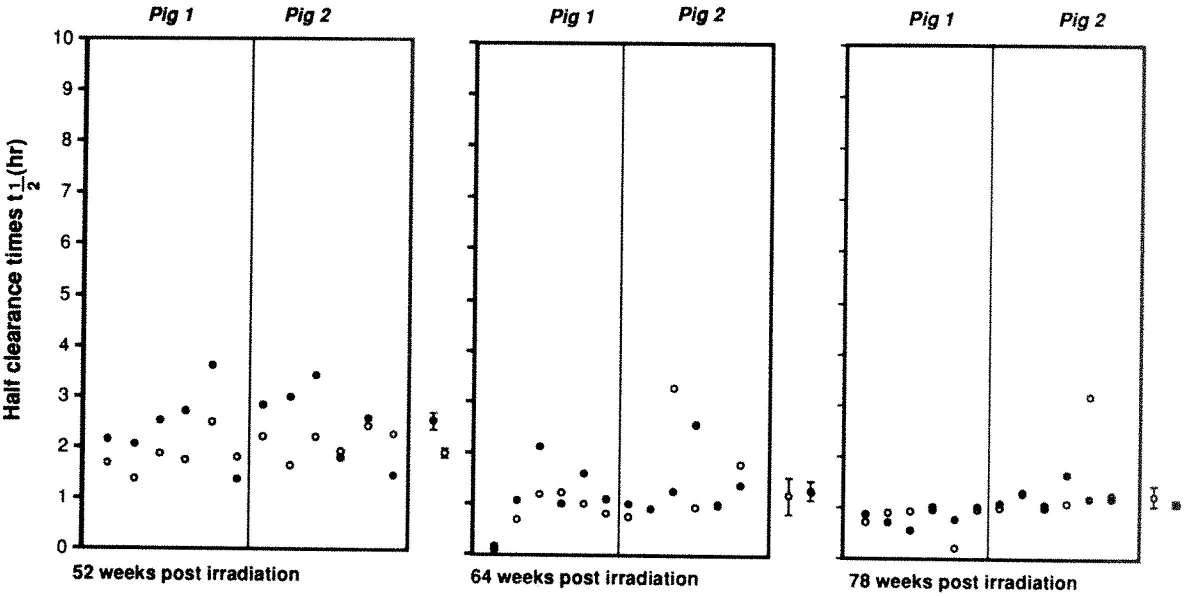

Figure 4. Individual and mean half clearance times ($t_{\frac{1}{2}}$ h) of each lymph clearance determined in irradiated (●) and non-irradiated (○) skin at intervals of 52, 64 and 78 weeks after a single dose of 18 Gy of X rays.

Table I. Mean half clearance times (±SE) in hours for each pig in both irradiated and unirradiated sites at intervals post-radiation

Weeks post-radiation	Pig 1		Pig 2	
	Irradiated	Unirradiated	Irradiated	Unirradiated
3	2.22±0.64 ($n = 5$)	1.71±0.32 ($n = 5$)	1.29±0.07 ($n = 6$)	1.46±0.16 ($n = 6$)
6	2.38±0.43 ($n = 6$)	1.23±0.9 ($n = 6$)	3.25±0.5 ($n = 6$)	1.41±0.11 ($n = 6$)
9	3.96±0.8 ($n = 4$)	4.22±0.91 ($n = 5$)	5.37±1.14 ($n = 5$)	4.55±0.98 ($n = 5$)
12	5.97±0.78 ($n = 5$)	3.33±0.13 ($n = 5$)	4.66±0.89 ($n = 6$)	2.94±0.33 ($n = 6$)
26	1.26±0.25 ($n = 6$)	1.05±0.11 ($n = 6$)	1.42±0.28 ($n = 6$)	1.03±0.05 ($n = 6$)
39	1.47±0.32 ($n = 6$)	1.09±0.08 ($n = 6$)	0.93±0.12 ($n = 5$)	0.89±0.14 ($n = 5$)
52	2.4±0.32 ($n = 6$)	1.82±0.13 ($n = 6$)	2.51±0.27 ($n = 6$)	2.11±0.1 ($n = 6$)
64	1.16±0.25 ($n = 6$)	0.84±0.14 ($n = 6$)	0.82±0.06 ($n = 6$)	0.79±0.11 ($n = 6$)
78	1.34±0.23 ($n = 6$)	1.43±0.36 ($n = 6$)	1.24±0.07 ($n = 6$)	1.47±0.31 ($n = 6$)

second wave, at 52 weeks, corresponded with development of dermal and subcutaneous atrophy (Baker et al, 1989).

The finding of reduced lymphatic function in unirradiated skin, and hence X ray impaired skin lymph drainage both within and beyond the field of irradiation, was unexpected and not the experience of other investigators (Moustafa & Hopewell, 1979; Young & Hopewell, 1982) who, under identical experimental conditions, have demonstrated blood flow changes in irradiated skin but not in the intervening normal skin. An explanation for the observed lymph flow abnormalities is likely to relate to the anatomy of lymphatics in the pig, which drain horizontally across the flank towards limb roots (Saar & Getty, 1964), whereas the blood supply is segmental in arangement (Donovan, 1975) and drainage does not pass through irradiated and unirradiated skin sites. "Control" unirradiated sites were chosen on the ipsilateral flank for lymphatic clearance measurements because of the risks of X ray damage from the exit dose on the correlation flank.

It has been suggested (Hopewell, 1986) that the main site of injury to the vasculature from X rays is at the base of the dermis. This would further explain the lymph flow abnormalities found in unirradiated skin. It also indicates that impaired tracer clearance from the sub-epidermal sites was as much a result of damage to deep lymph collectors, *i.e.* in base of dermis, with a secondary effect on superficial lymphatics, as it was of direct injury to superficial lymphatics. This theory is supported by observations in skin irridated with ^{90}Sr/^{90}Y. This source of radiation produces maximum effect at the skin surface with sharp attenuation throughout the dermis. Interestingly, ^{90}Sr/^{90}Y does not produce oedema despite high skin surface doses (Hopewell, 1990). Superficial initial lymphatics are passive vessels composed only of endothelium, whereas subcutaneous lymphatic collectors possess smooth muscle and are capable of contractions which actively propel lymph onwards (Mortimer, 1990). This function may be impaired following irradiation.

Non-invasive measurements of dermal thickness, using pulsed ultrasound, have shown a significant increase in the thickness of the dermis skin at 6 weeks after irradiation with 18 Gy (Baker et al, 1989). At this time there was no discernible oedema, although this did become clinically evident at 9 weeks after irradiation when the increase in dermal thickness reached a maximum. This was associated with a significant increase in skin stiffness as measured by a dermal extensometer (Baker et al, 1989). After the resolution of the oedema, the mechanical properties of irradiated skin were not markedly different from those of the unirradiated skin until 39 and 52 weeks after irradiation when there was another rise in skin stiffness. Therefore, the two waves of impaired lymphatic clearance appear to correlate well with a measurable increase in skin stiffness.

The finding of impaired lymphatic clearance at 6 weeks, before the onset of any measurable alteration in the mechanical properties of the dermis and a reduction of blood flow, suggests that lymphatic insufficiency is a cause and not a result of those other changes. Oedema is a striking macroscopic observation at 9–12 weeks after irradiation. Its development is presumed to result directly from radiation damage to blood vessels. The formation of oedema always indicates a relative or absolute failure of lymph drainage (Foldi, 1969), because one of the principal functions of lymphatic vessels is to control homeostasis and provide an overflow route for excessive interstitial fluid. The presence of oedema should increase colloid clearance through local diffusion, so the observation of reduced colloid clearance, before and during the phase of oedema, suggests that impaired lymph drainage is contributing to the formation of oedema. The increased permeability of lymphatic vessels may lead to the immediate leaking of colloid from these vessels as soon as entry is gained (Hudack & McMaster, 1933). The subsequent high interstitial fluid pressure may have "obstructed" lymph vessels, thereby further impairing lymph drainage.

Skin stiffness returned to values comparable with those obtained in unirradiated skin as the oedema resolved. A further marked increase in skin stiffness occurred at 39 and 52 weeks after irradiation. Impairment of colloid clearance at 1 year may relate to transient changes in the properties of the interstitial tissue. A change in the compliance of tissue may influence the ability of the interstitium to clear tracer and not relate to a direct effect on lymph vessels. Connective tissue changes are a consequence of skin irradiation. Connective tissue changes in humans are known to be an important factor preventing the regeneration of lymphatic vessels (Eloesser, 1923) and in the late onset of lymphoedema (Olszewski, 1985).

Injured lymph vessels usually regenerate very efficiently (Danese et al, 1962) and no method can totally guarantee the induction of permanent lymph stasis. The regenerative ability of lymph vessels varies with the consistency of the connective tissue through which the lymphatics must grow. Van den Brenk (1957) noted a slowing of regeneration in lymphatics after 20 Gy and suggested that this was because of the associated fibrosis, although it might equally have been caused by the effect of radiation on cell proliferation. Endothelial cells have a slow turnover, hence, damage to such cells will only be expressed slowly after irradiation (Hobson & Denekamp, 1984). No information exists on the cell kinetics for the lymphatic endothelium.

There have been no previous studies exploring the influence of X rays on the function of the lymphatics in the skin. Cox and Reinhold (1979), using subcutaneous injections of ^{51}Cr-HSA, investigated the effect of ionizing radiation in the rat, although this model does not exhibit similar radiation effects in the skin to man. Their studies demonstrated a longer half clearance time within irradiated areas. They concluded that this reflected local secondary congestion due to inflammation with the lymphatics remaining unaffected.

Considering that radiation is targeted on the lymphatic system in the treatment of cancer and that radiotherapy is the most important risk factor for lymphoedema following breast cancer treatment (Kissin et al, 1986), it is strange that there has been so few investigations of the effect of X irradiation on lymphatic function. The complicated pathogenesis of lymphoedema can be illustrated by experimental studies. Das et al (1981) demonstrated that only two out of six dogs receiving a block dissection of the lymph nodes, followed by radiotherapy, developed lymphoedema whereas all surviving dogs (10 out of 15) who received radiation before surgery developed lymphoedema at 1 year.

The pattern of early and late impairment of lymph drainage in the patient studies parallels the changes seen in human skin following irradiation. The development of post-mastectomy lymphoedema often manifests in two stages: an initial and transient oedema immediately following surgery and radiotherapy, and a second progressive lymphoedema developing 1–5 years after treatment (Olszewski, 1973). The reason for the delay in the development of permanent lymph stasis has never been explained. However, the observations recorded in these studies suggest that it may relate to the time taken for tissue damage to progress to a critical level sufficient to impair lymphatic function.

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Radical radiotherapy for 28 cases of mucosal melanoma in the nasal cavity and sinuses

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Abstract. Mucosal melanoma is rare and is traditionally treated by radical surgery. A retrospective survey was made of 28 cases of malignant mucosal melanoma of the nasal cavity and paranasal sinuses treated by definitive radiotherapy. Initial complete regression was observed in 22 out of 28 cases (79%). Absolute local control by radiotherapy alone was achieved in 17 out of 28 cases (61%) but follow-up was limited in many cases by early death due to metastatic disease; actuarial local disease-free survival was 49% at 3 years. The approach of radical radiotherapy for melanoma of this site can be justified on the basis of the local control achieved, low treatment morbidity in patients who are typically elderly and the propensity to disseminated disease. Doses of radiotherapy required to achieve local control need to be radical; the influence of dose per fraction is uncertain.

Malignant melanoma arising from the mucosa of the nasal cavity and paranasal sinuses is undoubtedly rare, constituting only about 5% of malignant tumours at this site (Holdcraft & Gallagher, 1969; Lederman, 1969; Logue & Slevin, 1991) and consequently the number of cases seen in any one centre will be small. In contrast to cutaneous melanoma, mucosal disease generally occurs in an older age group with 80% (Freedman et al, 1973) to 90% (Lund, 1982) presenting in the sixth to ninth decades.

The traditional approach to treatment has been surgical using wide *en bloc* excision. The basis for this approach derives partly from dogma that melanoma is radioresistant and also from the abundant experience of excision for cutaneous melanoma. Because of its rarity and the bias towards surgical management, the reported experience of using radiotherapy for mucosal melanoma is extremely limited, with its application usually restricted to locally advanced tumours given with palliative intent only. This inevitably provides a poor guide to the radioresponsiveness of mucosal melanoma.

Melanoma arising in the nasal cavity and sinuses has a marked propensity for systemic spread. Indeed, it has been suggested that mucosal melanoma is essentially incurable, irrespective of the treatment modality used (Freedman et al, 1973). It follows that the aim of treatment should be directed towards achieving local control with minimal cosmetic and functional disability. We report 28 cases of melanoma arising from the nasal cavity and sinuses treated with definitive radiotherapy in order to assess the usefulness of this approach.

Patients and methods

There were 42 cases of melanoma arising from the nasal cavity and sinuses registered at the Christie Hospital between 1961 and 1985. A retrospective study was made of the 28 cases in which radiotherapy was used as the definitive treatment. The excluded cases were two arising in the nasal vestibule, six with distant metastases at diagnosis, five treated with palliative radiotherapy due to locally advanced disease and concomitant serious medical illness, and one treated by radical surgery. There were 16 female and 12 male patients with a median age of 65 years (range 48–79 years). In 16 cases the tumour was seen to be arising from the nasal cavity and in four cases from the sinuses (ethmoid in two, maxillary antrum in two). In the remaining eight cases the disease was too extensive at presentation to determine the precise site of origin. Survival was expressed in absolute terms with none of the deaths less than 5 years post-treatment accepted as intercurrent. None of the cases were lost to follow-up.

Local disease-free survival was calculated using the life-table method (Peto et al, 1977). However, the life-table method is valid only if censoring is non-informative. Censoring cases of mucosal melanoma that were locally controlled but died early with metastases probably overestimates the true potential for long-term local control by radiotherapy.

Histological diagnosis was made by biopsy in all cases. A review of the original pathology was undertaken at the Christie Hospital in 23 out of 28 cases. It is conceivable that melanoma arising in these sites could be metastatic rather than primary. The diagnosis of primary mucosal melanoma is substantiated by the finding of adjacent *in situ* change. As the specimens were limited to biopsy material only, this information was not available. However, none of the cases had a

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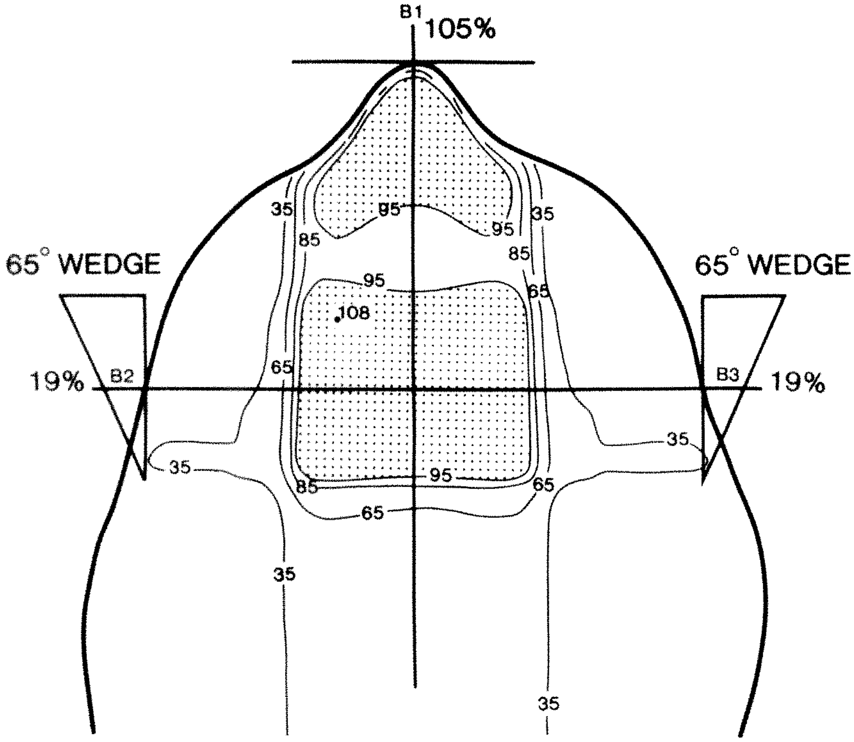

Figure 1. Typical radiotherapy isodose plan on a central horizontal contour (below eye level) showing the dominant anterior field with a pair of steeply wedged fields (behind lateral orbital rim) to compensate for dose fall-off posteriorly. The shaded area represents 95–105% of tumour dose.

known background of cutaneous melanoma. Immunohistochemical techniques were not used.

Radical radiotherapy was given by a beam-directed technique using megavoltage photons. In 25 cases the treatment was with an anterior field with (Fig. 1) or without lateral retro-orbital wedged fields to compensate for dose fall-off posteriorly, and in three cases by an anterior oblique wedged pair of fields. The tumour dose prescribed was 50–55 Gy in 15 or 16 daily fractions over 20–21 days except in two cases in which the dose was 45 and 47.5 Gy in 8 fractions over 9 days. Treatment interruption because of toxicity occurred in none of the cases.

Results

The crude 5-year survival was 17.9% (5/28) with a median survival of 26 months. Local control by radiotherapy is outlined in Table I and illustrated in Fig. 2. Initial complete regression was noted in 22 out of 28 cases (79%). Sustained local response for at least 12 months was seen in 17 out of 23 (74%) assessable cases (excluding the five early deaths due to metastases). Absolute local control by radiotherapy alone was achieved in 17 out of 28 cases (61%) but obviously follow-up was limited in many of these cases. There was no radiation necrosis recorded.

Three patients had surgery for residual or recurrent disease. Two of these died within 12 months with locally active disease, but the other patient survived for 76 months, dying from an oesophageal adenocarcinoma. No post-operative complications were noted in these three patients previously treated with radical radiotherapy.

In eight cases, cervical lymphadenopathy developed in the course of their disease. In three of these eight patients distant metastases were apparent, whilst a further three had persistent local disease. The other two patients received irradiation to the nodes, each dying less than 5 months from the time of nodal treatment with persistent nodal disease and lung metastases.

In 14 cases, death was ascribed to metastatic disease, documented sites being brain, bone, liver and lung.

Table I. Status of 28 cases of melanoma in nasal cavity or sinuses following definitive radiotherapy

Status	No. of patients
Disease-free at 5 years (alive 60 months; alive 90 months; dead 86 months, myocardial infarct	3
Local control, died of metastases after 12 months	9
Local control, died of metastases within 12 months	5
Local recurrence after 12 months	5
Local persistent disease or recurrence within 12 months	6

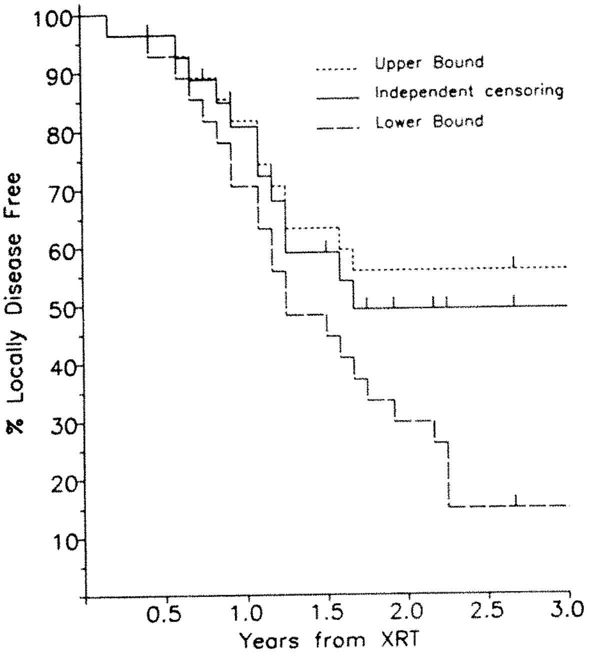

Figure 2. Local disease-free survival (solid line). Logical bounds on the sample estimate are inserted to show the two extreme non-observable events; local failure *never* occurs following death from metastases (dashes); local failure *always* occurs immediately following death from metastases (broken line).

Discussion

The crude 5-year survival rate for the 28 patients was 17.9%, which confirms the poor prognosis for mucosal melanoma owing to the marked propensity for distant metastatic spread. The broad aim of treatment is to achieve local control without disfigurement. However, the definition of local control is rendered imprecise as the length of follow-up is curtailed in many cases by early metastatic death. The usefulness of radiotherapy can, however, be gauged by an initial complete regression rate and sustained local response for at least 12 months in over 70% of cases. This is similar to previous reports of radiotherapy-induced initial complete remission rates for mucosal melanoma of 62% (Gaze et al, 1990) and 72% (Harwood & Cummings, 1982). These figures seem to compare favourably with those achieved by primary surgery of 65% (Freedman et al, 1973).

In this series, the radiotherapy was well tolerated, with no treatment interruption because of toxicity and no normal-tissue necrosis. For what is an elderly group of patients, the morbidity associated with primary radiotherapy is likely to be significantly less than with a surgical approach even when modern reconstructive techniques are used. Moreover, surgical "salvage" does not seem to be prejudiced by prior radical radiotherapy in terms of morbidity.

Prophylactic nodal irradiation for these mucosal melanomas is not recommended. Of the eight patients who developed cervical lymphadenopathy, six had either concomitant local disease or evidence of distant metastases and none of the eight cases survived for more than 24 months after primary radiotherapy.

Historically, melanoma has been considered radioresistant. Consequently, radiotherapy has generally been advocated and reserved for the treatment of advanced tumours and essentially with palliative intent (Shah et al, 1977), thus reinforcing the dogma. Clinical interest in radiotherapy for melanoma has been revived by recent radiobiological studies. Melanoma cell lines have been described as displaying a typical broad shoulder to their survival curves (Dewey, 1971) suggesting a high capacity to repair sublethal damage. Numerous studies then purported to show an advantage in using radiotherapy schedules with a "high" dose per fraction (Habermalz & Fisher, 1976; Hornsey, 1978; Overgaard, 1980). In one study (Hornsey, 1978), for example, a fraction size of 4–8 Gy was claimed to be associated with better local control than 2–3 Gy. However, it is apparent that much of this advantage could be construed as being due to the manifestly different biological doses used; not surprisingly, doses of 35–50 Gy in 7–10 fractions gave better results than doses of less than 35 Gy in 10–12 fractions.

Radiobiological studies have proceeded to demonstrate that melanoma cells show a wide variation in radiosensitivity. The *in vitro* surviving fraction following 2 Gy for cells isolated directly from human surgical specimens ranged from 0.14 to 0.62 in one study (Rofstad et al, 1985); moreover, melanoma cell survival curves displayed a broad shoulder for some but were almost exponential in others. These *in vitro* results are not necessarily representative of human tumour behaviour but overall they do not seem to conflict with the heterogeneity in radioresponsiveness observed in the clinical setting. Indeed, it is of interest that six of 19 primary tumour cultures of human melanomas gave survival fractions at 2 Gy above the range seen with various carcinomas analysed (Rofstad et al, 1987); this proportion matches the 20–30% poor clinical response reported in our study.

It can be concluded that melanoma of the nasal cavity and sinuses can reasonably be treated by definitive radiotherapy. The level of local control in this study was achieved with radiotherapy doses that were "radical" in the sense of being at normal tissue tolerance. The contribution of the dose per fraction characteristic of the schedules used (3–3.5 Gy in the majority of the 28 cases) and indeed the "short" overall treatment time of 3 weeks cannot be discerned. Surgery can be considered for patients with recurrent local disease who remain apparently free of metastatic disease.

Acknowledgments

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Technical note

Attempting to increase the sensitivity of the plain film for ureteric calculi; use of the full bladder

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(*Received November 1990 and in revised form April 1991*)

Keywords: Plain abdominal radiograph, Ureteric calculi

Although up to 90% of ureteric calculi are radio-opaque, the accuracy of plain films for their detection is surprisingly poor (Bloom et al, 1988). A case is presented where a vesico-ureteric calculus was visible only when the patient was radiographed with a full bladder. A radiograph taken with an empty bladder allowed bowel loops to fall down into the pelvis and obscure the calculus. Performing the abdominal radiograph with a full bladder rather than post-micturition potentially avoids this problem and may be useful when following up patients with ureteric calculi.

Case report

A 37-year-old male was admitted with severe right sided colicky abdominal pain radiating into his groin. A plain abdominal radiograph demonstrated a small calculus at the right pelviureteric junction (Fig. 1). An intravenous urogram was performed 12 h later by which time the calculus had impacted at the right vesico-ureteric junction (Fig. 2). 24 h later the patient was virtually pain free and a plain abdominal radiograph failed to demonstrate the calculus, suggesting it had been passed (Fig. 3). Over the next 48 h the pain gradually worsened and a further film showed the calculus was still present and impacted at the right vesico-ureteric junction (Fig. 4).

Discussion

Reported accuracy of the plain abdominal radiograph for the diagnosis of ureteric calculi is remarkably poor. Zangerle et al (1985) presented the plain abdominal radiographs of 120 patients (40 of whom had ureteric

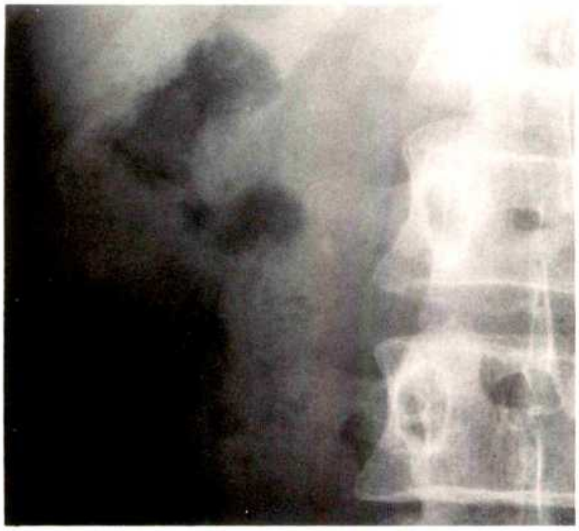

Figure 1. Plain radiograph of the right renal area showing a small calculus at the pelvi-ureteric junction (immediately inferior to the tip of the right transverse process of the second lumbar vertebra).

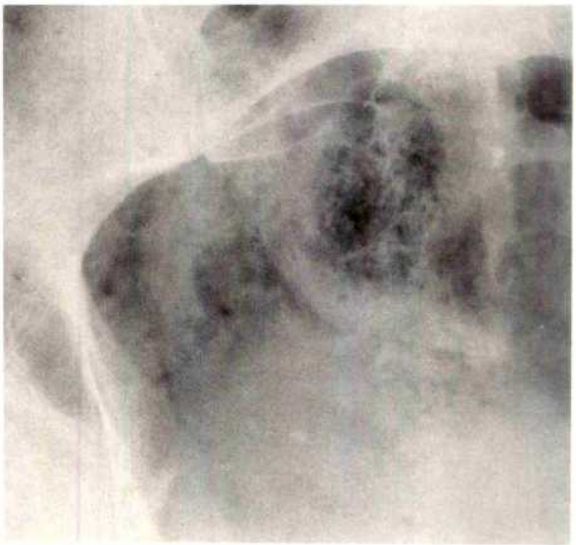

Figure 2. Preliminary film from the intravenous urogram series showing the small calculus at the right vesico-ureteric junction (about 2 cm medial to the ischial spine). Note the full bladder.

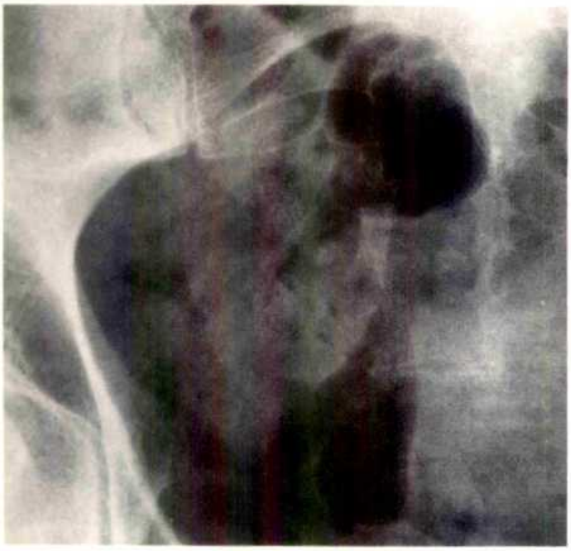

Figure 3. Plain radiograph showing the right bladder area and apparent passage of the stone. Note the empty bladder.

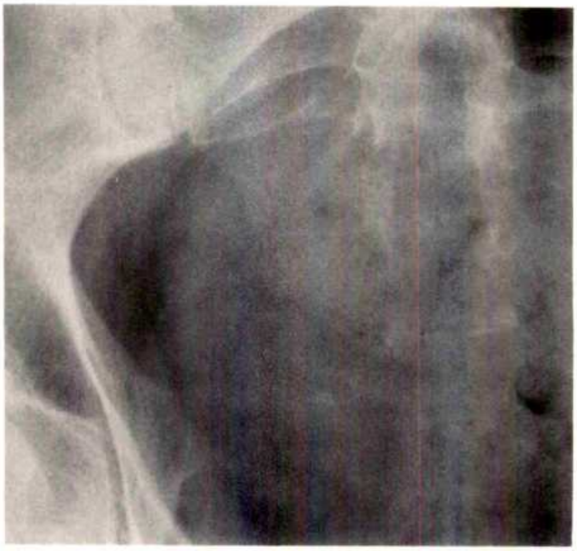

Figure 4. Plain radiograph of the right bladder area showing the calculus, still present at the vesico-ureteric junction. Note the full bladder.

calculi) to a radiologist and an emergency physician and asked them to predict which patients had ureteric calculi. The radiologist performed marginally better than the physician but overall they were correct in only 50% of cases. The authors noted that their readers rarely predicted calculi with great confidence (25–33% true positive rate) and falsely predicted calculi just as often (27–35% false positive rate). Roth et al (1985) performed a similar study with a series of 206 patients of whom a higher proportion had ureteric calculi (148 patients). In this study the reader achieved a sensitivity of 62% and a specificity of 67% in identifying the calculi. The authors commented that the intelligent selection of a diagnostic test depends on the purpose for which it is intended; confirming the presence of a disease requires a high specificity and excluding it requires a high sensitivity, neither of which is seen with the diagnosis of ureteric calculi on the plain radiograph. They concluded that the plain radiograph provides no more diagnostic information in these patients than does a careful clinical assessment and urinalysis, and that the diagnosis of ureteric calculi depends on intravenous urography.

The plain abdominal radiograph is legitimately used for the follow-up of ureteric calculi. However, calculi can be either concealed by overlying intestinal contents and bone or mistaken for other calcified structures, in particular phleboliths. Oblique films have been recommended in selected cases to help detect ureteric calculi overlying the sacrum (Gatewood & Berkowitz, 1990). Bloom et al (1988) described a characteristic truncated pyramid shape of some distal ureteric calculi, suggesting that this may aid diagnosis.

In the patient in this report the calculus was only visible in the distal ureter when the bladder was full. The plain film taken when the bladder was empty (Fig. 3) allowed loops of bowel to fall into the pelvis, the calculus becoming obscured by bowel contents. The plain radiograph of the urinary tract (KUB) may be taken following micturition, this practice is routine in some departments, especially to assess residual volume in patients with suspected bladder outflow obstruction, although its precise value is debated (Edwards & Beggs, 1987). More usually the radiograph is taken without regard to the state of the bladder (Bryan, 1981). Drawing on the experience of this current case it would seem useful to perform follow-up radiographs with a full bladder on patients with ureteric calculi.

A second, incidental, observation may be made on this case. Bloom et al (1988) when describing the truncated pyramid shape commented that they had never seen it elsewhere, other than in distal ureteric stones. This current case shows a calculus with a shape very similar to that described in their paper but clearly originating within the kidney.

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Case reports

Spontaneous fracture of the wire tip during breast localization

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Keywords: Fracture, Wire, Breast localizations

Needle localizations of radiologically suspicious but clinically impalpable breast lesions are being carried out with increasing frequency as a result of the National Breast Screening Programme. At our institution, the Nottingham Lesion Location Set (Mediplus Ltd, Bourne End, Bucks) has been used, without complication, for at least 50 such procedures (Fig. 1). It comprises an 18 gauge (G), or 21 G cannula, a fine needle localization wire which is fed through the cannula during initial positioning and a 20 G blunt-ended cannula which is introduced over the wire by the surgeon in theatre to facilitate identification of the wire tip. The following case report, undocumented to date, describes an unusual hazard of breast localization.

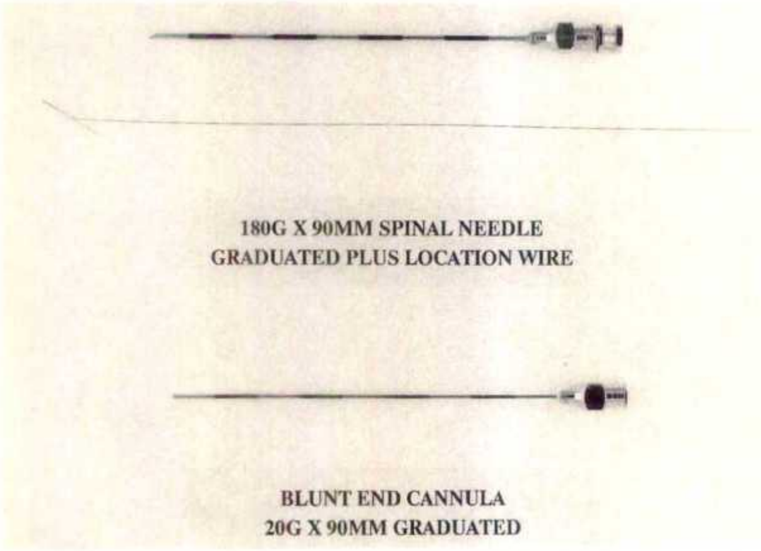

Figure 1. The Nottingham lesion location set.

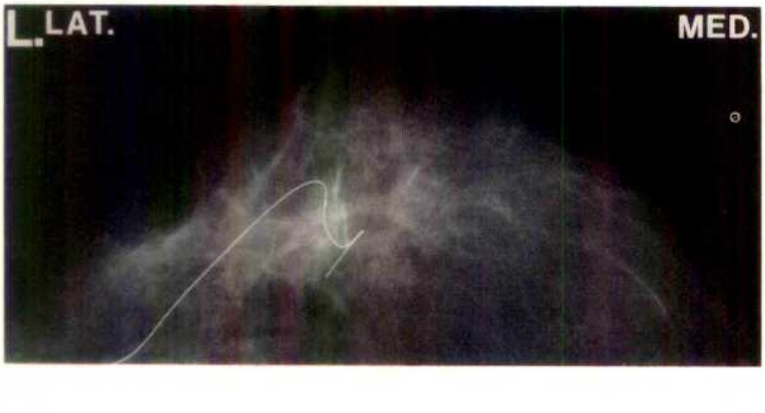

Figure 2. Post-procedure craniocaudal view.

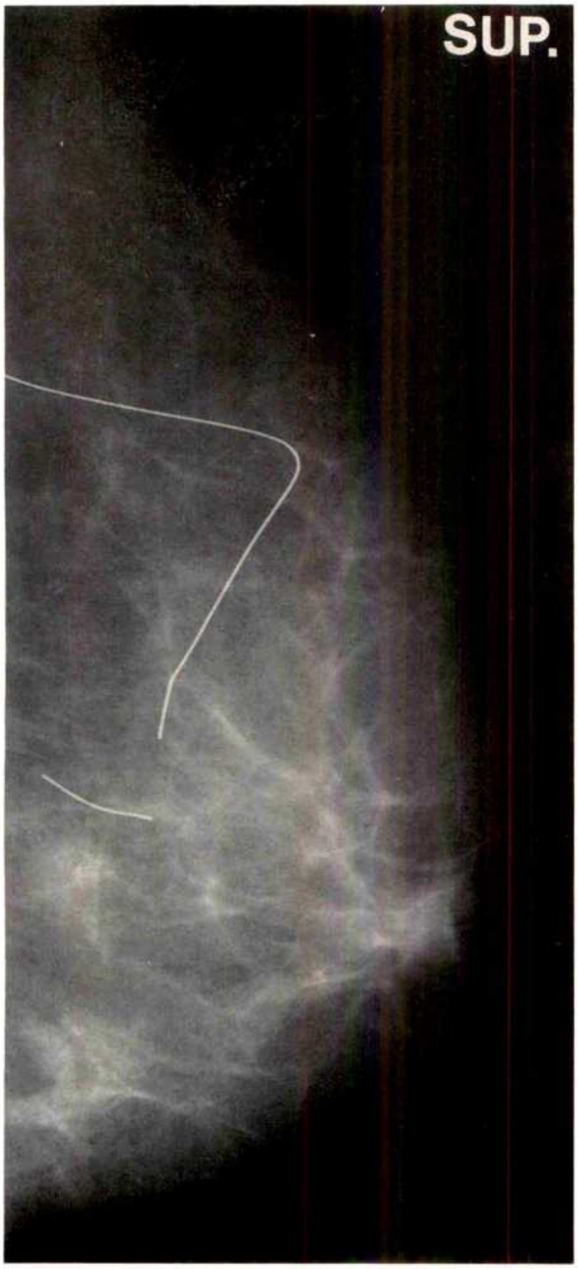

Figure 3. Post-procedure mediolateral view.

Case report

A 62-year-old woman was invited for routine breast screening at our unit. Mammography demonstrated a suspicious cluster of microcalcification within the left breast, but no palpable abnormality was found following recall for assessment. Stereotactic fine needle aspiration of the area yielded a cellular smear with features of carcinoma and she was referred for needle localization prior to surgical excision.

Using the Nottingham Lesion Localization Set, a localization wire was introduced into the region of microcalcification via an 18 G cannula without complication. No resistance to the passage of the wire was encountered and the outer cannula was withdrawn satisfactorily. On routine post-procedure mammography, the wire appeared well placed on the craniocaudal view (Fig. 2), but on the mediolateral projection it became apparent that the wire tip had fractured and was lying free within the breast (Fig. 3). Since the broken wire clearly could no longer be used by the surgeon to locate the lesion, a second localization wire was inserted into the area without event. The surgeon was informed of the situation and was able to successfully retrieve the free wire tip in the biopsy specimen. Both the microcalcification and the fractured wire tip were contained in the specimen radiograph.

Discussion

The Forrest Report predicted that there would be a biopsy rate of 1.5% in the prevalence round of the National Breast Screening Programme resulting in 19,137 biopsies annually (Forrest, 1986). Even at the current biopsy rate of 1.1% in the National Breast Screening Programme, (Vessey, 1991) a large number of biopsies for impalpable abnormalities requiring pre-operative localization are being performed. Numerous wire localization kits have become available over recent years; their various designs, methods of implementation, and individual merits have been well described (Frank et al, 1976; Kopans & Deluce, 1980; Homer, 1985; Feig, 1988). Reported complications of this normally straightforward procedure include migration of the wire following insertion (Bristol & Jones, 1981; Davis et al, 1988; Owen & Kimor, 1991) and transection of the wire tip during surgery (Homer, 1983). However, to date, no record has been made of spontaneous fracture of the wire tip. The standard technique was used; the wire was inspected prior to insertion and no problem was encountered during the procedure. In this case the fracture was presumably related to a defective wire, which was unrecognizable prior to insertion. The situation is easily recognizable provided good quality mammograms are routinely taken and carefully checked following the procedure. The placement of a second wire into the region allowed localization of both the mammographic abnormality and the faulty wire tip.

The manufacturers were informed of this case and although they had been aware of problems with the wire they had not encountered spontaneous fracture during localization. They have made modifications to improve the wire. A high quality mono-filament 36 gauge wire with a heat annealing process at the bend is now used and two crimps have been introduced to show the length of wire to be inserted. All old stock will be replaced.

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Afferent loop obstruction diagnosed by sonography and computed tomography

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(*Received February 1991 and in revised form May 1991*)

Keywords: Afferent loop obstruction, Sonography, Computed tomography

Although obstruction of the afferent loop following Billroth II gastrectomy is uncommon, it causes a rapid onset of severe abdominal pain, non-bilious vomiting and at times may become lethal if complicated by perforation and peritonitis. However, the diagnosis is sometimes difficult to establish by conventional biochemical and radiological means. We present one case in which both sonography and computed tomography (CT) were very helpful in establishing the early and accurate detection of this life threatening condition before surgery.

Case report

A 69-year-old female, who had previously undergone a partial gastrectomy and Billroth II reconstruction, was admitted with a 2 week history of right upper quadrant pain associated with nausea. There was a palpable mass in the right upper quadrant. Laboratory data on admission revealed normal values for haemoglobin, haematocrit, serum amylase, total birilubin, lactate dehydrogenase (LDH) and serum glutamate oxaloacetate transaminase (SGOT). The white blood cell count was 9800/mm^3. An upper gastrointestinal series showed non-filling of the afferent loop and a poor patency of the efferent loop. Upper gastro-intestinal endoscopy identified a small gastric remnant with a patent efferent loop and a blind pouch with a very small opening, thought to be consistent with an obstructed afferent loop. Abdominal sonography demonstrated a tubular cystic mass extending from the liver margin downwards and crossing over the aorta to the left abdominal cavity (Fig. 1). There were internal echoes in the mass, believed to be emanating from the valvulae conniventes of either the duodenum or the small intestine (Fig. 1). The mass was also shown between the superior mesenteric artery and the aorta (Fig. 2). There was no dilation of the intra- and extra-hepatic bile ducts and the pancreatic duct was also of normal calibre. Under sonographic guidance, the cystic mass was punctured and the serous fluid was collected. The amylase level observed in the collected fluid was extremely high (144 300 U/l). Because of the shape and position of the mass and the previous history of a Billroth II operation, the possibility of afferent loop obstruction was suggested. CT demonstrated two cystic abdominal masses which merged caudally (Figs 3 & 4). 5 days after admission the patient was clinically jaundiced (total birilubin 6.2 mg/dl). An emergency laparotomy was performed which revealed approximately 1 m of jejunum herniating behind a kinked afferent loop. A conversion of the Billroth II gastrojejunostomy to a Roux-en-y gastrojejunostomy was performed. The patient was discharged 18 days after the operation.

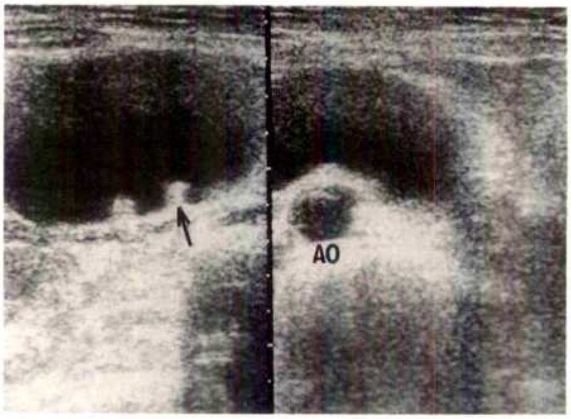

Figure 1. Transverse section on sonography. The mass crosses over the aorta. Note the hyperechoic internal echoes, suggesting a "keyboard sign" (arrow). AO = aorta.

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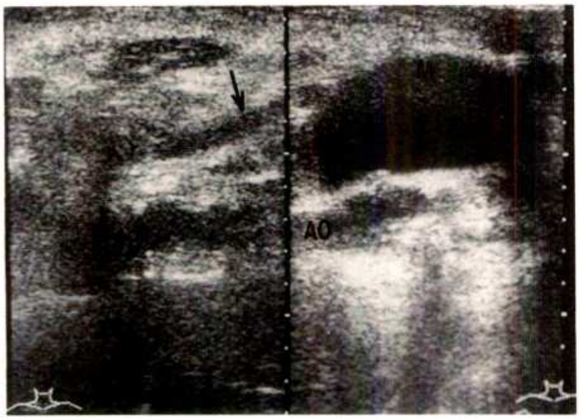

Figure 2. Sagittal section on sonography. The arrow indicates the superior mesenteric artery arching over a hypoechoic mass. M = mass; AO = aorta.

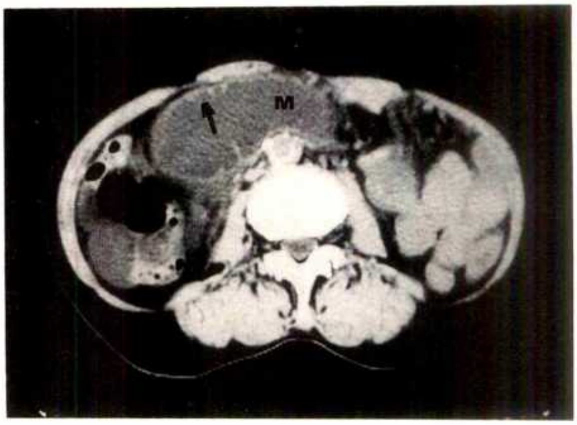

Figure 4. Slightly caudally, the masses are continuous, suggesting a U-shaped mass. Note the small linear densities in the mass, projecting from the wall (arrow). M = mass.

Discussion

The obstruction of an afferent loop is considered to be an abdominal emergency needing diagnosis as soon as possible. If treated medically as acute pancreatitis, delay in operation is almost always accompanied by high mortality (Alawneh, 1980; Peretz & Simmons, 1983). In this case the patient's condition was relatively long standing, since she had a 2 week history.

The accurate diagnosis of afferent loop obstruction may be difficult to make pre-operatively using conventional methods. The upper gastrointestinal series only demonstrates non-filling of the afferent loop. Similarly, upper gastrointestinal endoscopy may be successful in visualizing the afferent loop in only 75–80% of patients who have undergone Billroth II gastrectomy (Safrony, 1972). However, early upper gastrointestinal endoscopy is an important part of the diagnostic evaluation. Identifying gastritis or recurrent carcinoma in the gastric remnant, noting the presence or absence of bile as well as the patency of the two limbs of Billroth II anastomosis is also important.

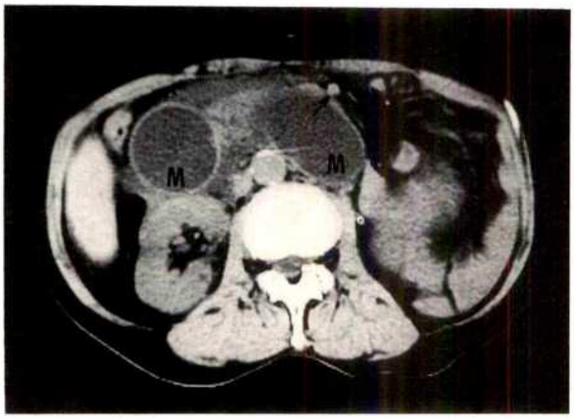

Figure 3. Computed tomography demonstrates dilated afferent loop as two distinct cystic masses. Note the anteriorly displaced superior mesenteric artery (arrow). M = mass.

As in our case, afferent loop obstruction has been diagnosed by sonography before exploratory laparotomy (Berger, 1980; Hopens et al, 1982; Matsusue et al, 1988). With sonography, the obstructed afferent loop appears as a cystic mass with the shape of the afferent loop, often U-shaped, so that it should be distinguished from pseudocyst of the pancreas or an enlarged gallbladder. Sonography of the mass may also demonstrate the "keyboard sign" or "stepladder sign", a term applied to internal echoes of the mass, emanating from the valvulae conniventes. A third clue may be the demonstration of the mass between the superior mesenteric artery and the aorta. Real-time imaging provides further information concerning the presence or absence of bowel motility.

Computed tomographic appearances are pathognomonic (Gale et al, 1982; Swayne & Love, 1985). Since CT is performed in the axial position, the obstructed afferent loop is demonstrated cross-sectionally as two round cystic masses which are continuous caudally, suggesting a U-shaped mass. The masses are uniform in size owing to the equal pressure within the afferent loop (Swayne & Love, 1985). The most convincing feature may be seen in the lowest section through the mass, in the area of the transverse portion of the duodenum. In our case small linear densities were seen projecting from the wall into the fluid filled centre. These are caused by the valvulae conniventes in the obstructed loop. On CT, the anteriorly displaced superior mesenteric artery should also be identified between the mass and the abdominal wall. This allows differentiation between a dilated afferent loop and a pancreatic pseudocyst.

We suggest that both sonography and CT should be regarded as imaging methods of choice in patients with clinically suspected obstruction of an afferent loop, since both investigative modalities present highly characteristic patterns.

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Scintigraphic detection of abdominal hernias associated with continuous ambulatory peritoneal dialysis

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Keywords: Scintigraphy, Peritoneal dialysis, Hernias

Continuous ambulatory peritoneal dialysis (CAPD) is an increasingly popular method of renal replacement therapy. There are many recognized abdominal complications including the leakage of dialysate fluid into abnormal sites (Steiner & Halasz, 1990). This may occur internally into the hernial sacs, the abdominal wall or the pleural cavity, or externally around the Tenckhoff cannula, or even via the female genital tract (Khanna et al, 1981).

Whenever possible, pre-existing hernias are repaired before commencing CAPD, as the raised intraperitoneal pressures involved can precipitate incarceration (Rubin et al, 1982). In addition, approximately 18% of patients will develop hernias during treatment (Johnson et al, 1987). Indirect inguinal, incisional, umbilical, ventral and diaphragmatic hernias are all described (Francis et al, 1984).

A common clinical problem is that of patients presenting with generalized swelling of the anterior abdominal wall, scrotum or labia. Localization of the abnormal communication is often not possible clinically. This report concerns nine patients presenting over a 3 year period in whom peritoneal scintigraphy was employed to detect the site of the leak.

Patients and methods

Nine patients on CAPD were referred for scintigraphic evaluation after developing soft tissue swelling of the anterior abdominal wall, scrotum or labia. No patient was known to have a pre-existing hernia and no hernias were apparent on clinical examination. A total of 10 examinations were performed.

A dose of 70 MBq of ^{99}Tc^{m}-DTPA was injected into a 1 dm^3 bag of dialysate. This was run into the peritoneal cavity over 10–15 min via the indwelling Tenckhoff cannula. Imaging was performed using a large field of view scintillation camera with counterbalanced detector and an all-purpose low energy collimator. The camera was interfaced to a dedicated computer.

Initial imaging was carried out for 20 min in the erect position centred over the symphysis pubis. Images were acquired at intervals of 5 min with frames of 500 000 counts. If no hernial sac was demonstrated then repeat images were performed at hourly intervals up to 8 h. No dialysate exchanges were made during this period.

Results

Patient details, scintigram results and operative findings are shown in Table I. Six males and three females were investigated using this technique. There was a wide age range (11–74 years) with a variable interval between the onset of symptoms and the duration of CAPD therapy (2 months to 6 years).

Inguinal leaks were demonstrated conclusively in eight of the nine patients. All were confirmed and treated surgically and all patients were able to continue on CAPD. The abnormal findings were left sided in four cases, right sided in two cases and bilateral in two cases. Inguinal hernias were present in four cases; all of these filled early (within 5 min) and often showed a clear

Table I. Patient details, scintigram results and operative findings

Patient	Sex	Age	Symptoms	Scintigraphic findings	Operative findings
1	M	12	Bilateral scrotal oedema	Right sided inguinal leak	Right sided patent processus vaginalis (found at 2nd operation)
2	M	76	Bilateral scrotal oedema	Right sided inguinal hernia	Right sided indirect inguinal hernia
3	F	11	Suprapubic and bilateral inguinal swelling	Inconclusive	Not explored (renal allograft 3 months later)
4	M	74	Bilateral scrotal oedema	Bilateral inguinal hernia	Bilateral indirect inguinal hernia
5	M	53	Bilateral scrotal oedema	Left sided inguinal hernia	Left sided inguinal hernia
6	F	66	Anterior abdominal wall swelling	Left sided inguinal leak	Left sided patent processus vaginalis
7	M	67	Bilateral scrotal oedema	Left sided inguinal hernia	Left sided inguinal hernia
8	M	74	Bilateral scrotal oedema	Left sided inguinal leak	Left sided patent processus vaginalis
9	F	12	Vulval oedema	1st study—right sided inguinal leak; 2nd study at 2 months—left sided inguinal leak	1st operation—right sided patent processus vaginalis; 2nd operation—left sided patent processus vaginalis

communication with the peritoneal cavity (Fig. 1). Indirect inguinal hernias were present bilaterally in one of these cases (Fig. 2), being larger on the left. Patent processus vaginalis was the cause of the leak in four cases (two males and two females). These often appeared on later images (up to 60 min), with little or no activity in the inguinal canal (Fig. 3). In one case, previous exploration of both inguinal regions had failed to locate a patent processus vaginalis subsequently demonstrated on the left side at scintigraphy. In another case the initial study showed a right sided leak. At operation a right sided patent processus vaginalis was ligated. When symptoms recurred 2 months later, a repeat scintigram showed a left sided leak which had not been apparent on the initial study. A left sided patent processus vaginalis was subsequently ligated.

In one patient the scintigraphic result was inconclusive, though there was a suggestion of abnormal activity in the upper part of the inguinal canal on both sides. CAPD was continued and a repeat study was planned 3 months later. However, in the meantime the patient

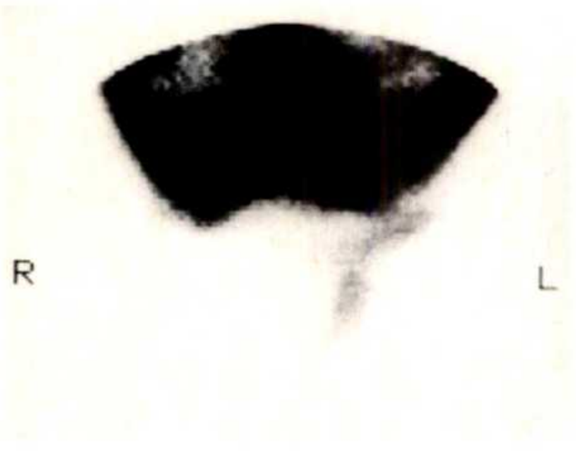

Figure 1. Unilateral inguinal hernia.

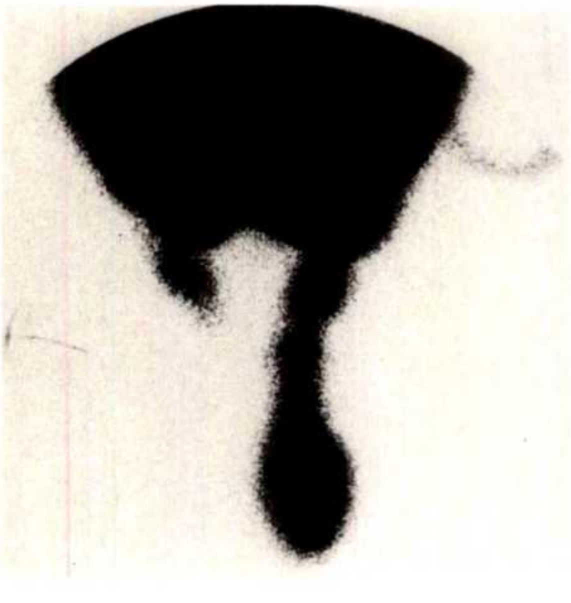

Figure 2. Bilateral inguinal hernias.

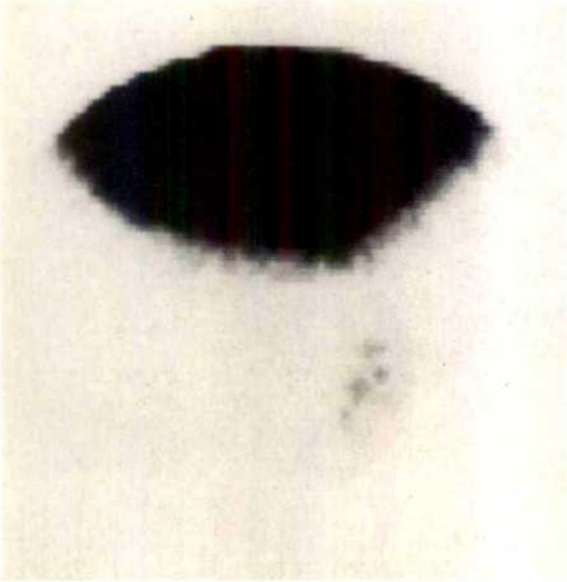

Figure 3. Delayed scan (40 min) showing patent processus vaginalis.

underwent successful renal transplantation. As a result no follow-up scintigram or surgical exploration was performed.

Discussion

CAPD is now a well established and a well tolerated treatment for chronic renal failure. Intra-abdominal pressure increases during dialysis (Gotloib et al, 1981) and can precipitate leakage of dialysate fluid into abnormal sites. The exact origin of any abnormal leakage can be obscured by generalized local swelling. This is particularly true in the anterior abdominal wall and genitalia, when scintigraphic evaluation can show an abnormality not evident clinically.

Leaks may also occur into the anterior abdominal wall around the Tenckhoff catheter, or at the site of previous catheter insertion (Brown et al, 1987). In this situation the scintigram may show abnormal uptake close to the site of the catheter. Fluid can also track away from the site of leakage, generalized genital oedema having been reported in relation to a periumbilical hernia (Orfei et al, 1984). The lateral projection is of value in the assessment of anteriorly placed leaks by projecting the abnormal activity clear of that in the peritoneal cavity.

The choice of radiopharmaceutical does not appear to affect substantially the usefulness of the images obtained. Technetium 99m DTPA, although not used in previous reports, has appropriate imaging characteristics. Other centres have used ^{99}Tc^{m}-labelled colloid preparations (Mandel et al, 1985; Johnson et al, 1987) and ^{99}Tc^{m}-pertechnetate has also been used successfully, despite the theoretical risk of image degradation from transperitoneal spread of the isotope.

Peritoneal scintigraphy has also been employed in the assessment of pleural effusions in CAPD patients owing to diaphragmatic leaks. It has been suggested that lymphatic uptake of particles up to 4–12 μm (such as colloid) will take place producing localized activity above the hemidiaphragm but not demonstrating the abnormal communication. It is also claimed that larger particles, such as ^{99}Tc^{m}-labelled macro-aggregated albumin (^{99}Tc^{m}-MAA), are more likely to show the site of leakage (Spadaro et al, 1982). However, in another report the reverse was true, with a diaphragmatic leak being clearly shown with ^{99}Tc^{m}-albumin colloid but not with ^{99}Tc^{m}-MAA (Walker & Fish, 1988).

Herniography using contrast agents has been performed as a primary investigative procedure in CAPD patients since 1972 (Gullmo et al, 1984). Relatively large amounts of contrast are used (up to 80 ml at 240 mg iodine/ml) which has to be removed later by dialysis. Small communications may be difficult to demonstrate and an extended imaging sequence over several hours is impossible. Computed tomographic (CT) peritoneography has been suggested as the investigation of choice, but this involves the use of large doses of contrast medium and may need several series of CT sections over several hours (Brown et al, 1987; Maxwell et al, 1990).

Instillation of dyes, such as methylene blue, into the peritoneal cavity has also been advocated. However, this may not adequately demonstrate a leak and can cause a chemical peritonitis.

In comparison, the scintigraphic technique described examines the entire area of interest and shows a high degree of sensitivity in detecting small volumes of leakage. It is safe, simple to perform, well tolerated and gives a low radiation dose to the patient (Johnson et al, 1987). CT peritoneography should be reserved for patients with equivocal scintigraphic findings.

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Spontaneous disappearance of a staghorn calculus

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Keywords: Calculus, Staghorn, Disappearance

A case of spontaneous dissolution of a staghorn calculus is presented. Disappearance of such a stone in the absence of long term antimicrobial therapy has not been described previously.

Case report

A 68-year-old insulin dependent diabetic woman was admitted to hospital with a 3 day history of malaise, confusion and vomiting. On examination she was pyrexial with tenderness in her lower abdomen. A clinical diagnosis of pyelonephritis was made.

Investigations subsequently confirmed *Escherichia coli bacteruria* and bacteraemia. Serum biochemistry revealed a urea level of 22 mmol/l, and a glucose level of 12.5 mmol/l. Serum calcium was normal. A plain abdominal radiograph (Fig. 1) and ultrasound examination showed a partial staghorn calculus in the upper pole calyces of the right kidney. The patient made an uneventful recovery following 1 week of intravenous and 3 weeks of oral antibiotics. She was readmitted after 7 months (for medical reasons) for elective percutaneous pyelolithotomy. A plain abdominal radiograph performed prior to pyelolithotomy (Fig. 2) failed to demonstrate the calculus. A renal ultrasound scan and a retrograde pyelogram (Fig. 3) also failed to reveal any evidence of the staghorn.

Discussion

Spontaneous dissolution of staghorn calculi is extremely rare and differs from the well recognized instability of solitary renal stones which may pass spontaneously. Dissolution of a staghorn in a patient prescribed hydrochlorthiazide (which lowers urine

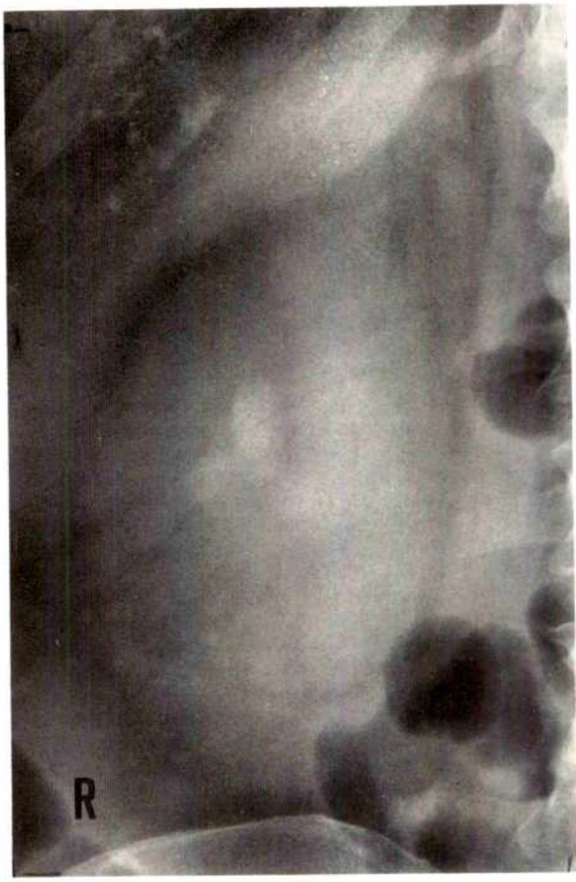

Figure 1. A plain radiograph of the right renal area showing a partial staghorn calculus.

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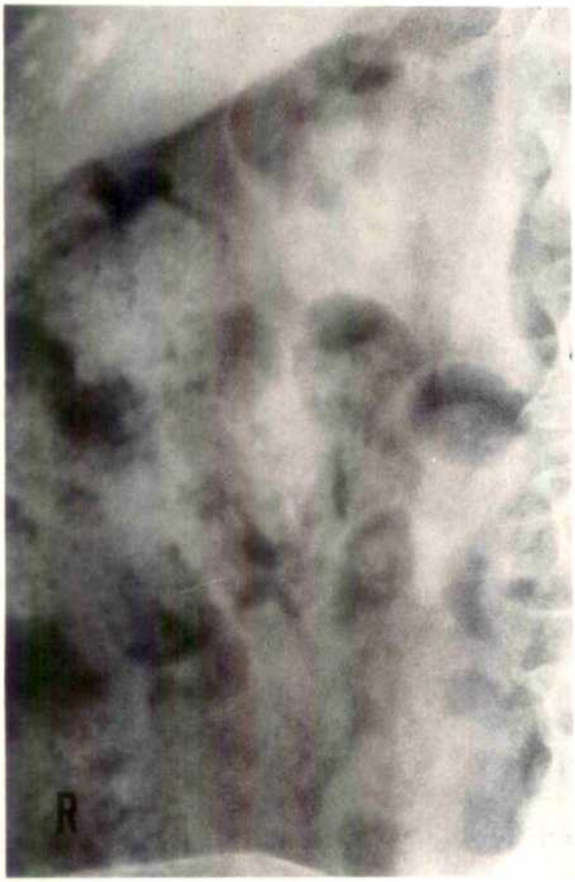

Figure 2. A plain radiograph of the right renal area 7 months after Figure 1, showing no residual calculus.

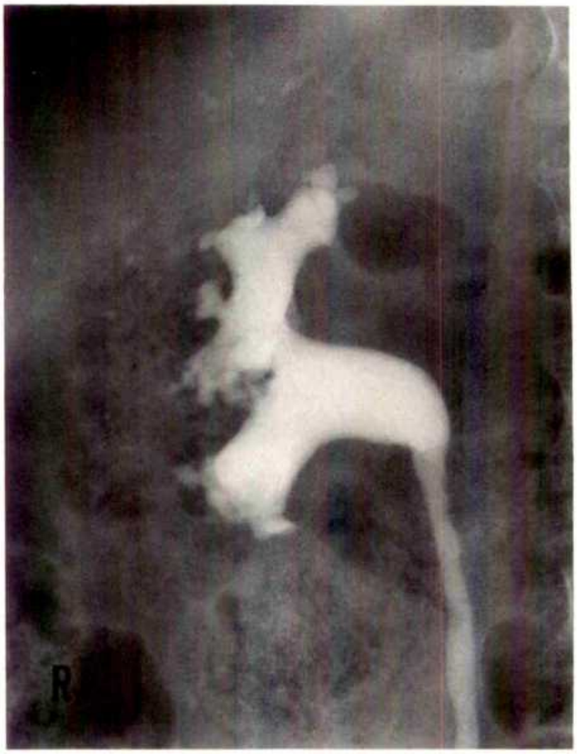

Figure 3. A right retrograde pyelogram using dilute contrast, showing features of papillary necrosis but no calculus.

calcium), antibiotics and ascorbic has been reported (Gaker & Butcher, 1986). There has also been a case reported of the disappearance of bilateral calyceal stones developing in a child immobilized for femoral fractures (Roder, 1982). Spontaneous extrusion of a staghorn into the abdominal wall (Breatnach et al, 1986) and extrusion causing a pyeloduodenal fistula (Cheatle et al, 1985) have been documented. Griffith et al (1979) describe reduction in size of infection-related stones in five patients whose urine sterility was achieved by long term antibiotics, and in a further four patients who received intermittent antibiotics and acetohydroxamic acid (which lowers urinary ammonia). A case of marked reduction in size of bilateral staghorn calculi after long term Trimethoprim is described (Griffith-Jones, 1990). A letter in reply to this article (Gleeson, 1991) echoes the opinion that long term urine sterilization by appropriate antibiotics may reduce calculus size. Definitive treatment of staghorn calculi is normally necessary to eradicate organisms from the urinary tract and to prevent such complications as pyonephrosis (Singh et al, 1973). This case reminds us that staghorn calculi can diminish in size after treatment of urinary tract infection and they can occasionally disappear.

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Case of the month

Mistaken identity of a neck mass

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(Received August 1990 and in revised form December 1990)

A 64-year-old woman presented at another hospital with a 4 year history of an asymptomatic left sided neck mass. On examination it was firm, non-tender and non-pulsatile. In addition she had an enlarged left tonsil. Computed tomography (CT) was performed (Fig. 1).

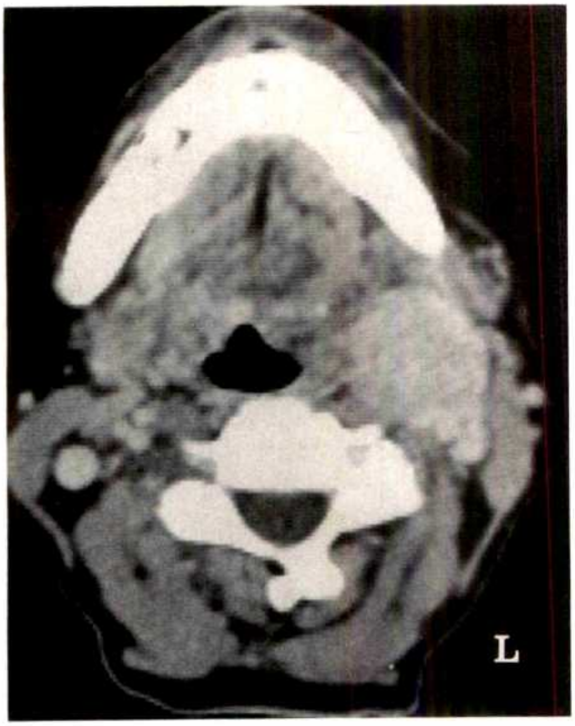

Figure 1. CT with intravenous enhancement at the level of C4 vertebra.

Following a left tonsillectomy surgical exploration of the neck was commenced. This was abandoned because of haemorrhage and the patient was referred for further investigation.

B-mode ultrasound showed an inhomogeneous mass of medium intensity echoes, splaying the left internal and external carotid arteries at the bifurcation. Doppler shift frequency signals were sampled at multiple sites within the tumour using two duplex machines (Acuson 128 5 MHz, Diasonics DRF 400 4.5 MHz). Figure 2 shows a representative recording. What is the most likely diagnosis?

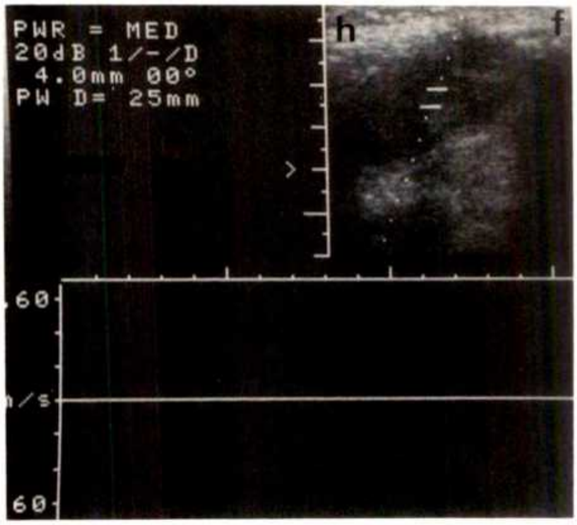

Figure 2. Duplex sonography of the neck mass, longitudinal section (Acuson 128).

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Keywords: Carotid body tumour, Computed tomography, Doppler ultrasound, Embolization

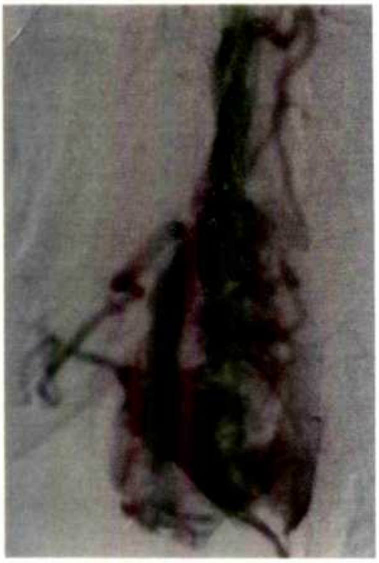

Figure 3. Digital subtraction angiogram left external carotid injection, lateral projection. An intensely hypervascular mass displaces the external carotid anteriorly.

On review CT showed a well defined homogeneous 3 cm mass in the left parapharyngeal space, extending from C1/2 to C4/5. The attenuation value was similar to that of adjacent muscle and enhancement of 50 HU occurred following an intravenous bolus of contrast (18.5 g of iodine).

Common carotid angiography showed a highly vascular mass at the bifurcation characteristic of a carotid body tumour. Left external carotid angiography (Fig. 3) showed that the tumour was fed by multiple branches and the larger ones were embolized with Ivalon (polyvinyl alcohol sponge) prior to surgical resection. Histology confirmed the diagnosis and the tonsillectomy specimen showed benign hyperplasia.

Discussion

Carotid body tumour is one of the commoner non-chromaffin branchial paraganglionomas with a wide age distribution and no sex dominance. Multiple tumours occur in 15% of all cases and are more commonly of the familial type. Malignancy occurs in up to 15% but histological diagnosis is not definitive (Lasjaunias & Berenstein, 1987).

The differential diagnosis of a mass at the carotid bifurcation includes pathologically enlarged lymph nodes (inflammatory, lymphomatous, metastatic), ectasia or aneurysm of the carotid arteries, carotid body tumour, branchial cyst and tumours of neurogenic origin (Lasjaunias & Berenstein, 1987).

In most cases B-mode ultrasound will distinguish solid tumours from branchial cysts and great vessel aneurysms. However, branchial cysts may be complex, containing debris, and schwannomas may contain cystic areas.

The ultrasonic appearance of the solid tumours is non-specific and duplex Doppler ultrasound has been advocated as a method of differentiation. Gritzmann et al (1987) using a 5 MHz probe recorded Doppler shift, indicating blood flow in three carotid body tumours; but no signal was obtained from cervical lymph node metastases. On the contrary, Mountford and Atkinson (1979) recorded Doppler shift (10 MHz probe) in pathologically enlarged lymph nodes.

In our case no Doppler signal was detected in the carotid body tumour, belying its true vascularity. Unfortunately, colour flow Doppler, which is more sensitive, was unavailable.

Our case illustrates that the absence of a Doppler signal in a tumour does not necessarily indicate avascularity. Slow blood flow below the minimum threshold for detection may still be present.

Similarly, the assessment of the vascularity of enhancing neck masses on CT is not clear-cut. Enhancement may reflect either high vascular flow or gradual extravascular accumulation of contrast, especially when an infusion technique is used. As a result enlarged lymph nodes, neuromas and carotid body tumours may all appear to enhance to a similar extent as major vessels (Som et al, 1985).

In this case the CT appearance had originally been interpreted as lymphadenopathy (possibly metastatic in view of the tonsillar enlargement). This pitfall might have been avoided if dynamic CT, as advocated by Som et al (1985), had been performed.

Carotid body tumour embolization may be performed either in patients unsuitable for surgery or to reduce tumour vascularity pre-operatively (Lasjaunias & Berenstein, 1987). Embolization should only be performed by an experienced specialist to reduce the risk of complications, the most serious of which is stroke.

Acknowledgments

We thank Professor P. J. Morris for allowing us to report this case and Dr A. J. Molyneux for details of the embolization.

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1991, The British Journal of Radiology, 64, 1165–1166

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(The Editors do not hold themselves responsible for opinions expressed by correspondents)

Fractionated high dose rate versus low dose rate cervix cancer regimens

The Editor—Sir,

I found the article on fractionated high dose rate (HDR) *versus* low dose rate (LDR) regimens for intracavitary brachytherapy for cervix cancer by Brenner and Hall (1991) to be most interesting, especially their use of 38 different sets of linear-quadratic (L-Q) model parameters in their computations. Their ability to fit the L-Q model to the observed late complications data from the Christie Hospital LDR clinical trial (their Fig. 8) was especially impressive.

Their analysis led them to two important conclusions about HDR cervix cancer therapy:

(a) At an HDR dose/fraction to point-A of 7 Gy, for courses of therapy which result in acute (and hence, probably tumour) effects equivalent to those expected with conventional LDR treatments, the expected incidence of Grade 2 or 3 late complications should be about 0.7% (asterisks in their Fig. 9). However, clinical experience from a recent survey of HDR techniques and outcomes indicates that this should be about 9%. (Orton, 1990; Orton et al, 1991).

(b) In order to fit the L-Q model (with their parameters) to the Christie Hospital late complications data, the authors concluded that doses to the critical normal tissues at risk of injury, typically rectum and bladder, were 0.35 times the point-A dose, whereas the survey data suggest that a more appropriate value for this factor "r" might be 0.6–0.75 (Orton, 1990; Orton et al, 1991).

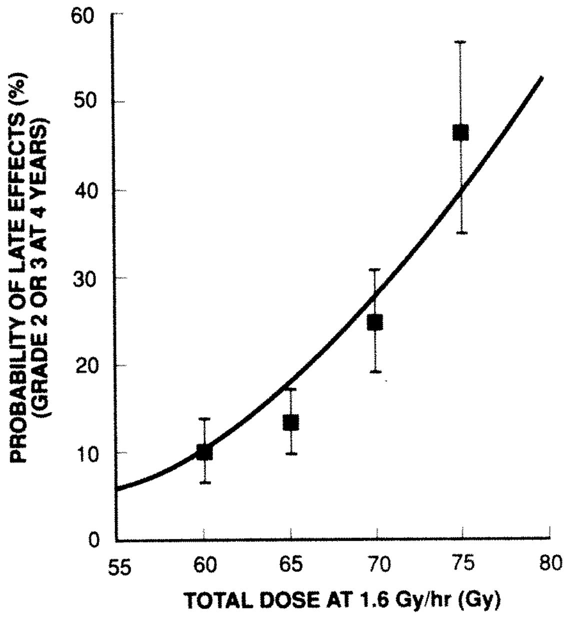

Figure 1. Probability of late effects (solid curve) derived from the Poisson model used by Brenner and Hall (1991) but with the new L-Q parameters (Table I), plotted as a function of the dose to point-A. The points in the figure are the Christie Hospital LDR clinical trial data plotted in Figure 8 of Brenner and Hall.

I wish to present an alternative L-Q model analysis of the Christie Hospital data, which is also consistent with the survey observations. What I have done is to determine L-Q model parameters which fit not only the Christie Hospital data (at 0.53 and 1.6 Gy/hr), but which also fit the survey observations (9% Grade 2 or 3 injuries at 7 Gy/fraction to point-A, and "hot-spot" rectal and bladder doses 0.6–0.75 times the dose to point-A). The parameters which "best fit" all these observations are shown, compared with the Brenner and Hall values, in Table I. As shown in Figure 1, the fit to the Christie Hospital 1.6 Gy/hr complication data is just as good as that achieved with the Brenner and Hall parameters (their Fig. 8).

Of special importance is what these new parameters predict for the variation of probability of late injury with fractionation. From their Figure 9, Brenner and Hall concluded that for equal acute effects, late-effect risks should decrease as the dose/fraction increases. This is illustrated by the lower curve in Figure 2. But this is contrary to clinical experience, since many HDR users have found it necessary to increase the number of fractions and/or reduce the dose/fraction in order to decrease complications (Joslin, 1980; Shigematsu et al, 1983; Utley et al, 1984). Although, for these three HDR users, only Joslin and Utley et al increased doses in order to

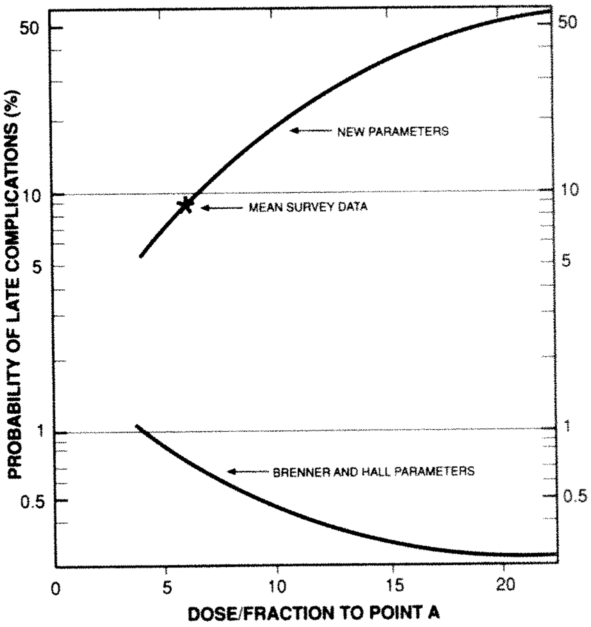

Figure 2. Predicted late effects (Grade 2 or 3 complications after 4 years) as a function of point-A dose/fraction for HDR treatments which are expected to produce equal tumour control and early effects. The lower curve corresponds to the values obtained using the Brenner and Hall (1991) L-Q model parameters, and the upper curve is obtained using the new parameters. The mean point-A dose from the survey data was 7.1 Gy (corresponding to a 9% complication rate), but this has been reduced 20% in this figure in order to be compatible with the two curves which were derived assuming that the parameter r (see text) was the same for LDR and HDR treatments. However, the survey data showed that r was 20% lower for HDR than for LDR (Orton, 1990; Orton et al, 1991).

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Table I. New L-Q model late-reacting tissue parameters which fit both the Christie Hospital LDR data at 0.53 and 1.6 Gy/hr, and the HDR survey observations (Orton, 1990; Orton et al, 1991), compared with the Brenner and Hall values (1991).

Parameter	New values	Brenner & Hall values
α_L (Gy^{-1})	0.062	0.084
β_L (Gy^{-2})	0.018	0.021
τ_L (mins)	32	23 or 252
ln (K)	4.58	3.6
r	0.68	0.35

keep tumour control rates constant. Furthermore, this is also contrary to the findings from the survey data (Orton et al, 1991), which showed that for HDR point-A doses ≤7 Gy per fraction the Grade 2 and 3 late complication rate was 7.6% (95% confidence interval 6.9%–8.2%), but for >7 Gy per fraction this increased to 11.2% (95% confidence interval 10.5%–11.9%). The difference was statistically significant, with $p < 0.001$.

The upper curve in Figure 2 shows that for acute effects comparable with those obtained with LDR therapy, the new L-Q parameters presented here not only predict more realistic HDR complication rates but also predict an increase in complication rates as dose/fraction is increased. The reason why Drs Brenner and Hall came to such different conclusions lies primarily with the value of r used in their fitting of the L-Q equation to the LDR Manchester data. The LDR data alone was insufficient to determine a definite "best-fitting" value for r, whereas the addition of a single HDR data point has made it possible to calculate a value of r which yields L-Q predictions more consistent with the HDR results observed.

Yours etc.,

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Authors' reply

The Editor - Sir,

Dr Orton's comments are both interesting and pertinent. As the linear-quadratic (L-Q) model increases in complexity from its early two parameter version ($\alpha/\beta_{\text{early}}$, $\alpha/\beta_{\text{late}}$), it becomes correspondingly harder to tie down all the relevant parameters. In our model of GYN HDR late effects, which Dr Orton has refitted using further data from his survey (Orton, 1990; Orton et al, 1991), there are no less than eight (sic) parameters ($[\alpha, \beta, T_{1/2}]_{\text{early}}$, $[\alpha, \beta, T_{1/2}, K, r]_{\text{late}}$).

Dr Orton has clearly demonstrated that by keeping six of our eight parameters essentially unchanged and by varying K and r (K the effective number of "tissue rescuing units" and r the ratio of "effective" bladder/rectum dose to the point-A dose) equally good fits to the data that we analysed can be obtained, as well as a good fit to the result of his survey. The value of r (0.68) that he obtained is in pleasingly good agreement with the results of the literature review shown in Table 1 of Brenner and Hall (1991); the consequences of such a value of r are illustrated in Figure 7 of this same paper. It is clear that we need even more data of the kind provided by Dr Orton's survey.

Notwithstanding the curve drawn by Dr Orton in his Figure 2, and attributed to Brenner and Hall (1991), nowhere did we conclude—and it would be wrong to so do—that "the late effect risk should decrease as the dose per fraction increases". Indeed, Figure 9 of Brenner and Hall (1991) clearly shows curves in which the probability of complications decreases with decreasing dose per fraction, which is just what Dr Orton observed in his survey.

What we suggested was that decreasing the dose per fraction whilst matching for equal early effects by increasing number of fractions and increasing the total dose, may lead to a small increase in complications. This is not the situation in Dr Orton's survey (Orton, 1990; Orton et al, 1991), in which the decrease in average dose per fraction (from ≥7.5 Gy/fraction to <7.5 Gy/fraction) is accompanied by an increase in average fraction number (3.9–5.4), but no change in the average total dose. In this case, the L-Q approach always predicts reduced late effects, which was what Dr Orton observed.

We conclude that the L-Q approach is robust enough to give the right qualitative trends, given adequate parameters. As the L-Q formalism becomes more complex with the addition of extra parameters such as $T_{1/2}$, r, potential doubling times, etc., the challenge will become to ensure the basic notions do not become lost in a mass of equations and numbers; we hope this interchange will contribute towards this goal.

Yours etc.,

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Proceedings of the British Institute of Radiology

Your CT scanner — are the bells and whistles worthwhile?

Abstracts of papers presented at a BIR meeting held at the British Institute of Radiology, 36 Portland Place, London, W1N 4AT, on Wednesday, 20 February 1991

Co-chairmen: Dr A. K. Dixon and Dr S. J. Golding

Image quality and radiation dose, by A. D. Sant
3D image reconstruction, by J. Gillespie
CT – assisted radiotherapy planning, by H. J. Dobbs. Abstract not received.
Measurement of bone mineral content, by J. E. Adams
Dynamic CT, by K. Miles

Image quality and radiation dose

A. D. Sant
Medical Devices Directorate, Department of Health, London

The Medical Devices Directorate of the Department of Health funds the assessment of a wide range of imaging systems. Imaging Performance Assessment of X-ray CT equipment is performed by the ImPACT group based at St George's Hospital, Tooting. ImPACT seeks to bridge the gap between what the manufacturer's brochure says and what the clinician sees, by obtaining information on the image quality of CT scanners for typical scan parameters. Six different types of clinical scan are used as a basis for comparison and the data published in the DH Blue Cover Report Series. Tables list the chosen scan parameters and associated measurements of image noise, spatial resolution and total absorbed dose obtained using head and body phantoms. In each table the scanners are ranked appropriately for the type of scan involved. A review of the most recently assessed scanners attempts to compare performance, in terms of absorbed dose and image quality, with cost. It is concluded that CT scanners are currently available which offer good image quality and low dose at relatively low cost. Data also demonstrates (1) how recent advances in detector efficiency can significantly reduce the total absorbed dose necessary for diagnosis, and (2) how decreasing from 2 mm to 1 mm slice width can increase the total absorbed dose values by up to 100% due to the problems of reducing pre-patient collimation down to the 1 mm level.

3D image reconstruction

J. Gillespie
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Computer software enabling three dimensional (3D) reformatting of CT data to be performed is now available from most manufacturers as a relatively low cost add-on to their CT systems. Although these software packages are simple to use and produce images rapidly, careful planning and attention to scan technique are essential if high quality 3D images are to be obtained. The patient must remain motionless during the scan procedure to avoid mis-registration artefacts. CT slice width must be kept as small as possible to optimize spatial resolution. Rapid sequence ("dynamic" incremental) scanning at reduced mAs levels reduces the scan time required to obtain a large number of CT slices as well as decreasing the radiation dose to the patient. Finally, a highly motivated radiologist and radiographer are essential. Preparation prior to initiating the 3D programme requires the radiologist to select those portions of the CT sections to be included in the 3D reformation, by use of the region of interest (ROI) facility. Within that region of interest those pixels to be incorporated in the reformation are prescribed by a variety of methods, pixels of bone density being the most commonly selected. Processing of this data is usually accomplished in minutes. The 3D image produced appears on the CT console screen and can be rotated almost in real time by use of the tracker ball. Selection of depth-encoded or surface reflectance modes alters the manner in which the 3D effect is conveyed. 3D reformatting has been found most useful in the evaluation of congenital and traumatic abnormalities of bone particularly in the cranio facial skeleton, pelvis and spine. Complex spatial relationships are displayed in an easily assimilated and reproducible manner, facilitating pre-operative planning. 3D reformatting of soft tissue structures is difficult and relatively limited using most 3D add-on packages although the display of enhancing intracranial lesions is possible. Independent work-stations offering sophisticated image processing facilities including 3D reformatting of soft tissue structures are commercially available but at a significantly increased capital cost. Such units do offer greater interactive facilities and can accept digital imaging data from other sources including MR. Other applications of 3D reformatting include design of customized joint prostheses.

Measurement of bone mineral content

J. E. Adams
Bone Disease Research Centre and Department of Diagnostic Radiology, University of Manchester

Quantitative computed tomography (QCT) is unique amongst methods of non-invasive bone mass measurement in providing for the separate estimate of cortical and trabecular bone mass in axial (vertebral body) and appendicular (forearm, tibia) skeletal sites. It is more usually applied to measure vertebral trabecular bone and the mineral content is expressed as a true density in mg/ml of mineral equivalent material, depending on the calibration phantom used (usually $K_2HPO)_4$ in fluid phantoms; hydroxyapatite in solid phantoms). A calibration phantom is required to correct for any scanner instability and beam hardening through the patient. QCT is now available in over2000 centres worldwide. The method is quick to perform and includes a lateral scan projection radiograph, followed by four 10 mm sections through the mid-plane of four vertebrae, generally T12 to L3 (10 min scan time, 10 min operator analysis time). With automation of selection of scan plane and region of interest (ROI), the time required is even shorter. As with the other quantitative techniques, consistent method and meticulous care are required in performing the measurements to achieve the high precision (1–3%) needed if BMD measurements are to be clinically useful. For single energy QCT a low dose technique should be used (80KVp, 70MA, 2s), to minimize radiation dose to an effective dose equivalent (EDE) of 30µsv (half the dose of a chest radiograph). Although marrow fat can cause some inaccuracies in single energy QCT BMD measurements, which can be corrected by a dual energy technique, this is at the expense of precision. Dual energy QCT is not essential to obtain clinically relevant BMD results in the vertebrae. Appropriate reference data must be available so that patients with reduced BMD and increased fracture risk can be identified. The measurement of BMD has an established role in certain diagnostic categories, including perimenopausal women, equivocal radiographic osteopaenia, patients treated with corticosteroids, and primary hyperparathyroidism. QCT would be an appropriate measuring technique to apply in these categories, and since it measures trabecular bone (eight times more metabolically active than cortical bone), QCT may be the most sensitive technique for monitoring changes in BMD caused by time or treatment. The purchase of QCT capabilities (£10,000–£15,000) would seem appropriate for centres where BMD measurements would provide a useful clinical service, and where the demand was insufficient to warrant equipment (SPA, DEXA) solely applicable to such measurements.

Dynamic CT

K. Miles
Department of Nuclear Medicine, Addenbrooke's Hospital, Cambridge

Dynamic computed tomography (CT) describes a rapid sequence of scans, usually performed after intravenous contrast administration. The sequence can be performed with table movement between data acquisitions (incremental) or with all the scans at the same level (single location). Technical considerations of both types of sequence are discussed. Incremental sequences are useful for studying blood vessels and in delineating vascular lesions, such as renal carcinoma, pancreatic adenoma and hepatic metastases. Avascular abnormalities, such as pancreatic necrosis, are also accurately demonstrated. The main advantage of single location sequences is that they enable derivation of functional information. Time-density curves can be constructed which will display temporal changes in attenuation, and hence iodine concentration, within any organ in the slice following an intravenous contrast bolus. These can be used for tissue characterization, for instance distinguishing various pancreatic tumours. Information about vessel flow, tissue perfusion and renal function can also be obtained. Examples of studies of intrarenal and hepatic blood flow are given. High resolution quantifiable functional images, such as a map of tissue perfusion, can also be derived.

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Book reviews

Advances in Breast Cancer Detection. Ed. by S. Brünner and B. Langfeldt, pp. xi + 195, 1990 (Springer-Verlag, Berlin), DM 135.
ISBN 3-540-52089-9

This monograph consists of the proceedings from the Fourth International Symposium on Detection of Breast Cancer which took place in Copenhagen during 1988. The contents are entirely concerned with radiological aspects of breast screening. Some distinguished American radiologists, Feig, McLelland and Sickles, have each made several contributions. Those who are interested in the subject will already be familiar with much of the presented work. Being published 2 years after the conference, some of the information is obsolete. Not surprisingly, the approach to quality assurance, as practised in the United Kingdom Breast Screening Programme, is far more sophisticated than is described in this book. The articles on the early experience with stereotactic fine needle aspiration will be of some interest, particularly as the technique is now becoming more widely available. It is surprising that physical examination, in combination with mammography, was still recommended for breast screening in 1988. Although screening mammography is regarded as being widely practised within the USA, it was unexpected to learn that uptake in a community only reached 38%, even with acceptance of the programme by the local medical society.

As well as a number of mediocre reports, this book contains some well referenced and useful synopses which may justify its purchase by those interested in breast screening.

G. H. Whitehouse

Clinical Radiology of the Breast. By Eric J. Roebuck, pp. x + 273, 1990 (Butterworth Heinemann, Kent), £27.50.
ISBN 0-433-00066-X

The author's aim in this textbook of breast radiology is to give not only a comprehensive account of radiological diagnosis of breast disorders, but also to discuss other aspects of the management of breast disease which are of importance and interest to radiologists. The first chapter, by Professor R. Blamey, is a summary of current practice in the diagnosis and treatment of breast cancer. In subsequent chapters, there is a detailed description of the normal development and anatomy of the breast with mammographic and histological correlation. There is a useful clear account of the recent classification of benign breast changes and their mammographic appearances suggested by the Royal College of Radiologists breast group. The discussion on the evidence for radiation induced breast cancers is concise and easy to read, as are accounts of mammographic technique and alternative means of imaging the breast. A method for interpretation of mammograms is described with emphasis on careful analysis of mammographic signs. The highlighting of 'key' features to look for with each of the main signs is particularly helpful. The quality of illustration is by and large good. However, photographic reproduction and printing of fine low density microcalcifications is a challenge for any publisher and some of the more subtle examples of lobular calcifications are not demonstrated clearly. The final chapters discuss the practice of mammography in the context of the team approach to modern diagnosis and management of breast disease, both in the symptomatic clinic and the screening service. The importance of quality assurance is emphasized and methods of measuring radiological performance in screening mammography, such as ROC curve analysis, are described.

There is a comprehensive list of up-to-date and relevant references at the end of each chapter. There are many useful line diagrams and graphs which complement the text and illustrations.

The author has succeeded in demonstrating that there is far more to the practice of modern breast radiology than reporting mammograms. This book represents good value for money and will complement existing atlases of mammography. I recommend it to both radiologists and clinicians involved in the diagnosis and management of breast disease.

M. J. Michell

Handbook of Ultrasound in Obstetrics and Gynaecology. Ed. by Asim Kurjak, pp. 360, 1990 (Wolfe Publishing, London), £120.00.
ISBN 0-8493-3253-2

This two volume multi-author text gives a very comprehensive view of the uses of ultrasound in obstetrics and gynaecology. Basic principles of ultrasound scanning are dealt with and the topic of safety of diagnostic ultrasound well discussed. It is somewhat disappointing, however, that there is no mention of the possible increased hazard from the use of transvaginal Doppler ultrasound. A comprehensive systematic review of the uses of ultrasound in early pregnancy, assessment of fetal anatomy, detection of fetal abnormalities, and detection of growth retardation are all comprehensively handled in volume 1. The role of fetal surgery and ethical and legal issues are also dealt with. Volume 2 discusses fetal echocardiography, invasive diagnostic procedures, Doppler ultrasound and the uses of ultrasound in gynaecological practice. The final chapter on transvaginal colour Doppler gives an up-to-date review of the place of this new development.

The book is extensively referenced and the illustrations are, on the whole, of a very high quality. Unfortunately, several similar books have been produced within the last 12 months and the potential purchaser is left with a difficult decision between several excellent texts. This book in its two volumes, relatively small in size, is easier to handle than its competitors and can be recommended for its comprehensive nature, extensive bibliography, and very up-to-date review of the subject.

D. W. Pilling

Chemotherapy of Gynecologic Cancer (Second Edition). Ed. by G. Deppe, pp. xv + 491, 1990 (Wiley & Sons Ltd, Sussex), $165.00
ISBN 0-471-56687-X

This book is aimed at gynaecologists, oncologists and other cancer specialists using cytotoxic drugs to treat the whole range of gynaecological cancers. It also includes the management of breast cancer.

The book is divided into 20 chapters, many of which deal with an individual site—vulva, vagina, cervix, endometrium, ovary, fallopian tube and breast. There is also a chapter on the chemotherapeutic management of gestational trophoblastic tumours.

The first three chapters are devoted to the principles of cancer chemotherapy including basic cell biology, such as the cell cycle, and pharmacological aspects. The latter includes the development of new drugs, the classification of cytotoxic drugs and their individual therapeutic efficacy in gynaecological cancer. A separate chapter concentrates on the management of adverse effects of chemotherapy. While this information can be found in any standard oncological textbook the third chapter, by a statistician, on the design, analysis and interpretation of chemotherapy trials, is a timely and appropriate reminder not only on the complexity of designing good clinical trials but also on the dangers associated with the interpretation of small non-randomized trials.

The major part of this book consists of individual chapters on the use of chemotherapy at each gynaecological site. These are review articles all written on a similar basis, first considering the activity of single agents and then reviewing combination chemotherapy. Hormonal treatments and innovative therapies such as multi-modal approaches are also comprehensively covered. Some chapters are naturally short, such as those on the chemotherapy of vulva and vaginal malignancies, fallopian tube neoplasms, sarcomas and lymphomas. The comparative rarity of cases in such areas means that most of the studies reviewed are extremely small and not significant. Clinical trials for carcinoma of the cervix and endometrium are also infrequent, giving little firm evidence of the value of chemotherapy beyond palliation. In contrast, many studies using chemotherapy for carcinoma of the ovary have been carried out and this is reflected in that the subject is covered in three chapters—the first on epithelial ovarian cancer, the other two on germ cell tumours and malignant ovarian stromal tumours. The final chapters are concerned with areas not covered in the individual site reviews such as chemotherapy for cancer in pregnancy, tumour markers and steroid receptors in endometrial cancer. In addition experimental approaches such as immunotherapy, DNA analysis of tumours and the use of monoclonal antibodies are also included.

Overall I found this a disappointing book. Most of the information can be found in any of the numerous books on gynaecological oncology already on the market. Some chapters are difficult to read, for example the section on combination chemotherapy in breast cancer has sentences which seem to be no more than a string of references. In addition, the information contained in some of the shorter chapters is of little practical value. However, for those gynaecologists who carry out their own chemotherapy and for the radiotherapist with a special interest in gynaecological cancer this book has some value both as an overview and as a good source of references. This book is probably too expensive for the individual but would be useful in a library.

H. LAMBERT

Intraoperative Radiation Therapy. Ed. by R. Dobelbower and M. Abe, pp. x+413, 1989 (CRC Press, Florida), £127.50. ISBN 0-8493-6846-4

This multi-author text reviews the current experience of intraoperative radiotherapy (IORT) at a number of American and Japanese centres and also at two European centres (Innsbruck and Pamplona) who are exploring this approach to improve localization. The technical logistic and biological problems associated with this technique are well described in a number of chapters from different centres. However, the general tone of the presentations represents points of view committed to further exploration of IORT and, thus, the book serves as an excellent guide to those planning to incorporate it in their own departments rather than a basis for objectively judging the potential of this approach for improving the practice of radiotherapy. The 33 chapters are not well coordinated and many represent very similar experiences of different centres. Therefore, there is a series of reports of preliminary pilot studies describing the use of IORT for almost every tumour site with results which are often claimed to be impressive, but which are extremely difficult to evaluate because of patient selection and lack of prospective control data. Most of the reports are on fairly small numbers of patients and all too often results are reported in terms of percentage recurrence within a field.

The overall message does come through that if intraoperative radiation therapy has any role in clinical practice it is likely to be as an adjuvant treatment following surgical resection, and also that the technique should be applied in association with more conventional external beam therapies.

The chapter contributed by one of the editors virtually covers the entire field on its own and is a thorough and succinct review. A telling phrase comes in his conclusions, "the concept of IORT is intellectually pleasing and intuitively acceptable . . .".

The level of international activity in this field clearly cries out for scientific evaluation in prospective randomized trials, and the details in this book do provide sufficient preliminary information to help in the design of these trials.

Generally, the book is well presented and there are many clear illustrations and only one or two which left me bewildered. The book is extremely expensive, a consequence perhaps of the limited number of radiotherapists who will be interested in buying it.

A. HORWICH

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BIR Bulletin

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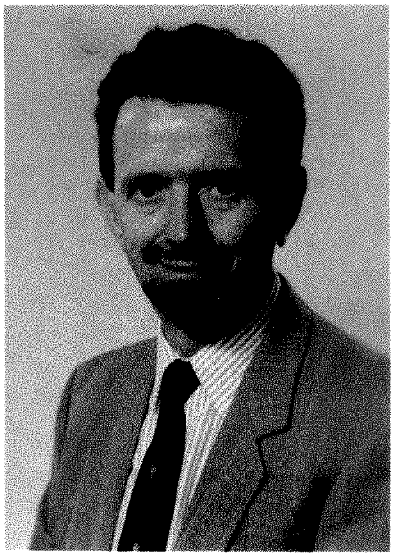
NEW PRESIDENT FOR THE BIR

Professor Stephen Lillicrap first joined the Institute's Council in 1979 as a scientific member with a background in radiation physics. His enthusiasm for physics was first kindled by attending evening courses, whilst at school, run by the Workers Educational Association where, in a run-down lecture room with bare floorboards, the wonders of nuclear physics were unveiled and he was "hooked".

Stephen Lillicrap describes himself as one who moves on slowly. Six years at undergraduate and postgraduate level at Imperial College, London were followed by 14 years at the Institute of Cancer Research and Royal Marsden Hospital at Sutton. He moved from his PhD topic, concerned with the galactic origins of high energy cosmic rays, to the application of physics to medicine and he found that the enthusiasm and support of his new colleagues at the Royal Marsden Hospital quickly dispelled any misgivingsthat he might of had. Val Mayneord, his new head of department, immediately had him recalculate his PhD results to determine and publish the natural background due to high energy cosmic rays; J C Jones, who sadly died in harness, patiently demonstrated the thoroughness of approach needed when accuracy is paramount; Nigel Trott convinced all newcomers of the importance of joining the BIR; and Brian Stedeford taught him the elements of his new trade of radiotherapy physics, which have been with him now almost 30 years.

The Institute of Cancer Research/Royal Marsden Hospital combination was, and still is, a very stimulating place to be, particularly for the younger scientist, with the Institute requiring a solid research output of physics applied to medicine and, at the same time, the hospital demanding value-for-money for the services paid for under an abatement arrangement. When Martin Fielden joined Jack Boag, the new head of physics, in 1965 there followed a fruitful 10 year period of collaboration between Martin and Stephen using the Institute's experimental linear accelerator to explore energy absorption and transfer processes following irradiation in DNA and other molecules of biological importance, using the technique of pulsed radioluminescence spectroscopy.

In 1977 Stephen moved to Bath to be both head of the newly formed Wiltshire Area Medical Physics Service and director of the University's Institute of Medical Engineering. More importantly for him it was clear that a similar academic physics/hospital service environment to that experienced at Sutton was being encouraged. He and his new colleagues felt fortunate to be welcomed as collaborators from the start by both scientific and medical communities, and were encouraged to forge research links across the physics and engineering schools of the University. In 1989 he became a founder member of the University's new School of Postgraduate Medicine set up to develop further the existing academic/medical research links in Bath. He describes his research interests now as exploring the niches of radiation physics for possible applications in medicine. The niches have included tailoring X-ray spectra to the patient, particularly for mammography, photon absorptiometry and scattering for bone-mineral assessment and X-ray flouresence for the detection of trace amounts of heavy metals in organs.



The BIR and the IPSM have been his major societies having served on the Council and Scientific Committees of both. He has contributed to the BJR sup-

☞

plements on Depth Dose Data and Radiotherapy Simulators. For the IPSM he is just finishing an enjoyable seven-year stretch on the editorial board of the journal *Physics in Medicine and Biology*, the last four years as Honorary Editor.

Since moving to Bath he has become involved in a number of advisory committees to the Department of Health, Home Office, Department of Trade and Industry, MRC, London Univesity, and grants committees of the CRC and MRC. Following the accidents, involving overdoses to patients, which occurred with linear accelerators in the early 1970s (and regrettably some since) he was asked to become convenor and secretary of the safety standards working group for radiotherapy equipment of the International Electrotechnical Commission. He feels that, in a quiet way, the working group has contributed significantly to safer radiotherapy equipment internationally. Like his predecessor, Charles Joslin, he finds collecting committees to be an addictive hobby and to date has not discovered a cure.

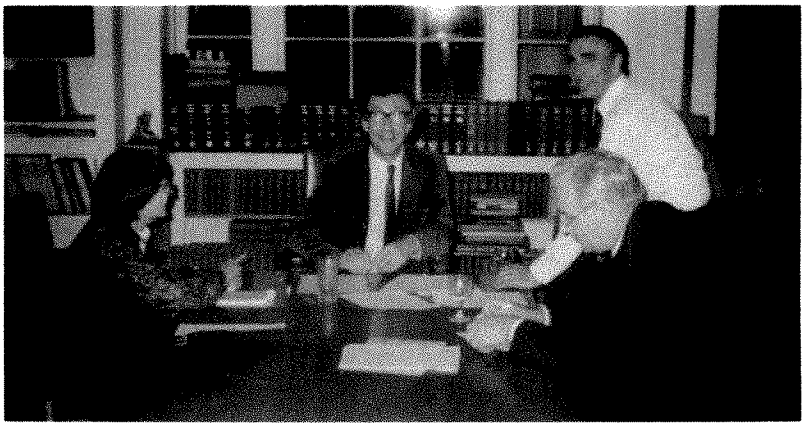
Outside the laboratory, Stephen has found himself the leader of church-based young people's groups called 'Pathfinders' for over 20 years in both Sutton and Bath. He retired, he says, when he realised that the bruises and sprains which go with the job were taking longer to heal with age. He appreciates the community atmosphere in country dancing and plays occasionally for a local caller - a far cry from struggling with Prokofiev in the college orchestra! An interest shared with all the family is a love of mountains and a week's fell-walking in the English Lakes is an annual feature. There is also vociferous family support for Bath rugby!

In perspective : a man of many parts

An appreciation of the life of Douglas Currie. 1921-1991

Douglas Currie joined the BIR as Caretaker and Steward in 1965 and retired in 1987, after 22 years exemplary service. He came when the expiration of our lease on 32 Welbeck Street seemed a distant prospect but stayed to see us established in 36 Portland Place, with the trauma of the move in August 1981 and the excitement of the official opening by Her Majesty the Queen on 11th February 1982 well behind us. He worked with four General Secretaries, took an increasing part in staff work at Annual Congresses and saw the covers of the Journal go from flimsy brown to stiff blue and white but just missed the move to glossy white and blue. I first met Douglas when he was mastering the arts of projecting slides (on the 9ft high platform in the Reid-Knox Hall, the handsome former Russian Chapel), arts which involved tact and self control when yet one more ill-mounted glass slide jammed in the projector. Monthly Thursday evening meeting, often preceded by a 45 minute discussion group with DMR and DMRT students, were a feature of Welbeck Street life, as were the refreshments before and after the main meeting: Douglas and his wife Betty then coped cheerfully and efficiently with 50 or more members crowding the narrow passages to the Library and saw that everyone went home refreshed. Douglas was born in Haddington, near Edinburgh, entered domestic service in his teens and worked for some years with Lord and Lady Forteviot in their castle in Perthshire. In the war he joined a Scottish regiment and served in Burma but contracted recurrent malaria and was sent home. His great love was the theatre and he was for many years an actor with the professional company Glasgow Unity, playing in Scotland and in England. On his marriage to Betty, he decided that the uncertainties of the professional actor's life were ill-suited to a settled home but in Haddington he took a great interest in amateur dramatics and wrote plays and sketches for the local company. Then, seeking work in London, he secured his appointment to the BIR. His perceptive dry humour and common sense made him a popular figure at No 32 but his dramatic talents were unknown to most of us until, in an emergency, he took over as Toast Master at the BIR dinner in 1980; he held this additional responsibility for several years, with much acclaim. When he retired to Haddington he took up amateur dramatics again, wrote a play about Mary Queen of Scots in her fourth centenary year, which won the Scotsman Award at the Edinburgh Festival, and another of his plays, a comedy, was performed at the Festival this year. Regrettably, his retirement was short: he was taken ill late in 1989 and underwent radiotherapy at the Western General Hospital in Edinburgh. Here the doctor in charge, seeing him, said "and what are you doing here, Mr Currie?", going on to tell the nurses how Mr Currie had kept him alert with cups of coffee during his days studying at the BIR. Douglas died in St Columbia Hospice on 21st January 1991. He is greatly missed by Betty and by all his friends in Haddington. Those long associated with the BIR will recall his courteous help and his engaging personality with respect and affection.

NIGEL TROTT



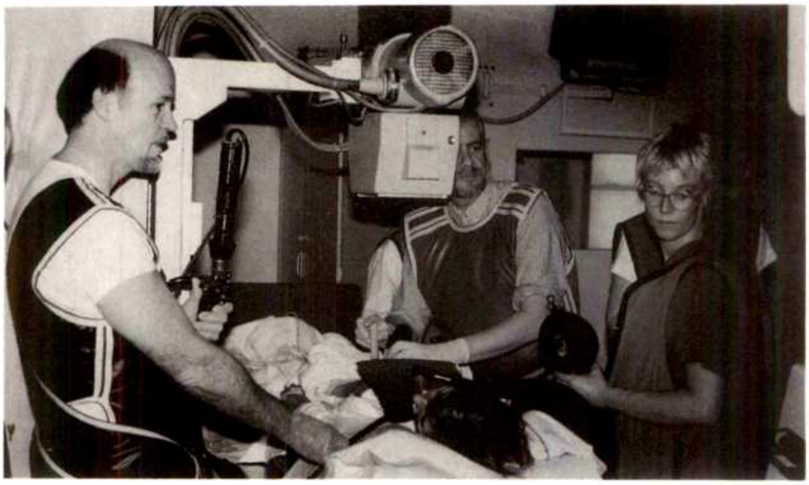
Douglas with (from left to right) Mrs Diana Jasper, Mr David Trapnell and Mr John Massey.

Nycomed Scandinavian Scholorship

March & April 1991

Report by Dr J. Tawlinson

The purpose of the scholarship was to gain further experience in interventional gastrointestinal radiology, to include the technique of endoscopic retrograde cholangio-pancreatography (ECRP) and related therapeutic procedures. Two Scandinavian centres were visited during the two month scholarship: Aarhus Kommunehospital, Denmark and University Hospital of Lund, Sweden.



Aksel Kruse (left) and Aksel Haubek (middle) combine endoscopic and ultrasound expertise to place a cyst-gastrostomy catheter via a percutaneous transgastric approach in order to drain a pancreatic pseudocyst. The patient is under general anaesthesia.

Aarhus Kommunehospital, Denmark

Five weeks of the 2 month period were spent in the endoscopic unit of this regional teaching hospital, under the direction of Aksel Kruse. Dr Kruse is a radiologist accomplished in all aspects of endoscopy, but he is most widely known for his expertise in ERCP, with personal experience of more than 10,000 examinations. Approximately 900 ERCPs were performed at Aarhus last year. The unit receives referrals from all over Jutland (the largest and westernmost portion of Denmark); as a result the ERCP service caters for a population of about 1.5 million.

During my stay the number of ERCPs weekly ranged from 15-20, the majority of which were interventional therapeutic procedures. This is consistent with ERCP practice worldwide, the advent of good quality ultrasound and computed tomography having largely dispensed with the need for purely diagnostic examinations. I saw a wide spectrum of pathology. Therapeutic procedures performed during my visit included sphincterotomies, dormia basket extraction of intraduct calculi, mechanical lithotripsy, endoscopic stenting of a variety of bile and pancreatic duct strictures and nasobiliary drain placement. It was exceptional for Dr Kruse not to access and drain obstructed bile ducts, so during my stay there were no percutaneous biliary drainages or combined percutaneous/endoscopic procedures. However, I saw one pancreatic pseudocyst drained using a combination of endoscopy and ultrasound guidance (photograph).

A major obstacle to learning ERCP is the side-viewing duodenoscope - the movements and techniques required bear little relationship to those needed for conventional forward viewing endoscopes. Optimal positioning of the instrument is crucial for successful cannulation of the ampulla. These fundamental aspects of ERCP have to be acquired before interventional procedures can be conducted safely. Plenty of "hands-on experience" at Aarhus facilitated the learning process. Dr Kruseis a master of the procedure but still retains a humble understanding of learning difficulties.

Laser procedures are also conducted in the endosocopy unit: several patients underwent laser treatment to recanalise obstructive oesophageal lesions. Those in whom laser therapy was inappropriate had their symptoms palliated by dilatation and tube placement. I saw four patients have palliative laser treatment to control haemorrhage from advanced rectal cancers.

Each day started at 8 am with a surgical meeting when cases admitted during the previous 24 hours were discussed. This was followed by a radiology conference with a review of current imaging investigations, including ERCPs from the preceding day. This ensured good liason between the radiological, surgical and endoscopic units.

On the few occasions when the endoscopic unit was quiet I took the opportunity to see the radiology department, including the local magnetic resonance unit. I delivered two lectures: one on the Himalayas; the other on a radiological topic - ultrasound features of gastrointestinal tract lesions.

University Hospital of Lund, Sweden

Three weeks were spent at Lund. The department of radiology is sited on three levels and subdivided into sections. I was mainly involved with the abdominal section under the guidance of Hans Stridbeck, the Chief of the section. However, I also spent several sessions in the experimental laboratory where Anders Lunderquist now works. He has retired from clinical duties but continues with research and to organize and execute training courses in interventional radiology.

The day starts early in Lund, with rounds at 7.15 am when the emergency films and relevant special investigations performed over the previous 24 hours are reviewed. This is in preparation for a later meeting with the clinicans. The long working day starts at 8 am with special procedures and finishes at 5 pm.

Although there has been a reduction in interventional procedures the department has a strong tradition in angiographic techniques. While Anders Lunderquist no longer has a clinical committment most of those working in the abdominal section have been trained by him at some stage in their career.

☞

I saw a range of angiographic procedures, including angioplasties, visceral angiography and embolizations. CT portograms were frequently performed in patients with malignant disease to assess the extent and number of hepatic metastases. There was a good spectrum of non-vascular intervention including renal and biliary drainages and percutaneous procedures on the gallbladder. The most interesting of these involved the rotary lithotrite - a device inserted into the gallbladder via a cholecystostomy. A rotating propeller then proceeds to reduce gallstones to a liquid slush within minutes.

Lund have pioneered the use of a variety of metallic expandable stents for a wide spectrum of conditions: including malignant biliary, venous and bronchial obsctruction and for arterial stenoses in selected cases. During my vist I was fortunate to assist Dr Krassi in utilizing them in combination to stent malignant oesophageal lesions.

In the experimental laboratory I assisted with a project involving the iatrogenic formation and stenting of porto-caval fistula in pigs. It is Dr Lunderquist's view that all interventional procedures should be animal tested: not only to see that they work but also to give the operator experience. Other experimental work included the trial of a high speed rotary lithotrite on gallstones surgically placed in the gall bladder and urinary bladder of anaesthetised pigs.

I was fortunate to be in Lund during an endoscopy teaching course. The ERCP workshops were on a practical basis which usefully complimented the experience in Aarhus. I was also able to attend and participate in some of the routine ERCP sessions.

In both centres there was ample opportunity to utilize library and word processing facilities. The departmental members were extremely hospitable and welcoming, immediately accepting me as part of the team and, without exception, always willing to teach and discuss ideas and techniques. I am deeply grateful to both Nycomed for sponsoring the visit and the Scandinavian centres concerned for the enormous contribution they have made to my endoscopic and interventional training.

BIRMINGHAM

(You'll be surprised at the change!)

Mention 'Birmingham' as a conference venue and many potential attendees will grimace at the thought of smoking chimneys, the 'spaghetti' junction and general grimey and industrial image of the 19th century 'Black Country' of which the city was such a major part.

The reality of modern Birmingham is very different. The 1980s were a time of massive investment in the city with the opening of the International Convention Centre (ICC) in April 1991. The ICC, will serve as the venue for Radiology & Oncology '92 — the BIR's 50th Annual Congress. Its eleven meeting halls, seating from 30–3000 people have been carefully designed and equipped with the very latest technology. MED X RAY is an integral part of the Congress and the ICC exhibition halls are well integrated with the conference rooms.

Birmingham now has direct flights from over 25 European cities and connections from New York and Toronto. It also has excellent road and rail links.

The accompanying persons programme includes excursions to Warwick Castle and Stratford-upon-Avon to visit Shakespeare's birthplace and the Shakespeare Centre. A tour to the Black Country Museum recreates a 19th century industrial village. The final tour is to Cadbury World in Bournville where participants will see chocolate products being made by traditional methods.

The City has a lively arts scene. Radiology & Oncology '92 delegates will be offered the opportunity to experience a concert in the magnificent Symphony Hall at the ICC. The concert will be given by the USSR Philharmonic Orchestra of Novosibirsk (programme details to be announced) and participants will also be invited to a post-concert buffet. The evening has been very generously supported by Schering Health Care Ltd.

Other cultural attractions in the city include the D'Oyly Carte Opera company, the Birmingham Royal Ballet (formerly the Saddlers Wells Royal Ballet), and the City Museum and Art Gallery with its famous collection of Pre-Raphaelite works.

The remaining organised social events include the BIR's Annual Dinner at the scenic Botanical Gardens in Edgbaston and the visit to the classic and modern cars of the Patrick Collection at Kings Norton followed by a buffet supper.

I hope the above has whetted appetites of what Birmingham has on offer. The Congress Advance Programme and Registration Form has now been circulated. Please address any queries, (technical or social) to either myself or my colleague, Elizabeth Carruthers in the BIR Conference Office.

I look forward to seeing you in Birmingham.....

Vanessa Whitehead
BIR Conference Manager

Information about the Nycomed Scandinavian Scholarship

The British Institute of Radiology invites applications for two Nycomed Scandinavian Scholorships.

These scholorships - generously funded by Nycomed (UK) Ltd - are to enable diagnostic radiologists of senior registrar or junior consultant status, preferably members of the British Institute of Radiology, interested in diagnostic or interventional procedures concerned with intravascular contrast media, to visit one or more academic departments of radiology in Scandinavia (Norway, Sweden, Finland, Denmark). A maximum of £5,000 will be available for each scholarship to permit two months of concentrated study free of financial constraints. The recipients will be responsible for their itinerary, travel, accommodation and insurance arrangements, subject to the approval of the BIR.

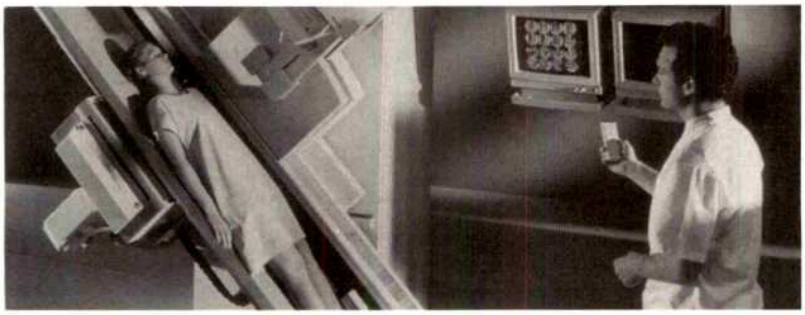
A condition of the scholarships is that a report of work undertaken, in a form suitable for publication in the Bulletin of the British Institute of Radiology, shall be submitted.

For further information please write to:
*The General Secretary, The British Institute of Radiology, 36 Portland Place,
London W1N 4AT*

Compact and Universal...

Philips have recently launched a new remote controlled universal system, the DIAGNOST 96. It uses the latest technology and is reliable and cost effective. It is compact with the lowest possible height at any tilt angle allowing easy patient access. It has a complete range of applications from routine examinations to special procedures.

The incorporated DSI provides quality images at reduced X-ray dose. Images are automatically optimized and simultaneously presented. An overview of 16 images can be displayed on the monitor for image review and selection.



Further information from Philips Medical Systems, Kelvin House, 63-75 Glenthorne Road, Hammersmith, London W6 OLJ. Tel. 081-741 1666. Fax. 081-741 7651.

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The SNIP is a complete radiometric laboratory, easily transportable for routine or emergency use. It will cater for germanium or stabilised sodium iodide detectors with standard pulse height analysis, multichannel scaling modes and quantitative and qualitative analysis. It will also perform as a PC based system.

The single or dual ratemeter and scaler-timer modes of operation support a wide range of detectors for precision, versatility and reliability.

Contact: Trever Nicholls, Southern Scientific Ltd, Old School House, South Street, West Tarring, Worthing, West Sussex, BN14 7NL. Tel. 0903 821178.

Ionising Radiations Metrology Forum (IRMF)

The IRMF has been formed for the exchange of information on available UK calibration and testing facilities and their efficient use in the UK to satisfy the requirements of the Ionising Radiations Regulations 1985 (IRR 85), and in particular the calibration and routine testing of devices used for radiation protection purposes. It is also intended that the IRMF will represent members' interests in discussions and correspondence with expert bodies, including those responsible for regulations and for formulating standards.

The activities of the Forum include the encouragement of good practice in measurement, including traceability to national standards, the organisation of regular meetings to discuss matters of common interest and concern, and the maintainence and promulgation of a register of UK calibration and testing facilities and services.

Contact Peter Christmas (Extension 6317) or Julian Hunt (Extension 6561)

BIR Calendar

Unless otherwise indicated, enquiries should be addressed to the Conference Manager, British Institute of Radiology, 36 Portland Place, London W1N 4AT (Tel. 071-436 7807).

Vascular systems imaging
January 24, 1992
Organizer: Dr J. F. Reidy

Radiosensitivity
February 11, 1992
Organizer: Dr M. Saunders

Quality standards in nuclear medicine
February 18, 1992
Organizer: Dr A. Smith

3-D image analysis in medical imaging
February 25, 1992
Organizer: Professor M. A. Smith

Megavoltage portal imaging
April 9, 1992
Joint meeting with IPSM
Organizer: Dr W. Jones

Radiology & Oncology '92
18–20 May 1992
International Convention Centre, Birmingham

Measurement Techniques for Ultrasound Exposure
July 1, 1992
Organizer: Dr F. Duck

The BIR Library is open weekdays 9 a.m.–5 p.m. (7 p.m. on Tuesdays and Thursdays).

The journal stock includes more than 100 titles. Though journals may not be taken out of the library, there is a photocopy service, also available by post or FAX. A list of current journals is available on request. Most books (excepting the historical collection) are available on loan.

BIR facilities are available for hire.

The rooms available include, the Lecture Theatre which holds up to 100 people in raked seating with excellent audio-visual equipment; the Siemens and Jan Lewando rooms and the Library.

BIR Company Subscriber Scheme

The BIR company subscriber scheme is aimed at all companies with an interest in radiology and allied sciences.

For an annual subscription of £300 p.a. member companies are offered an attractive benefits package. To find out why your company should join the leading edge companies listed below, please contact Mr Tony Hudson, Administration Manager, British Institute of Radiology, 36 Portland Place, London W1N 4AT. Tel: 071-580 4085.

AEA Technology
Wigshaw Lane, Culcheth
WA3 4NE. Tel. 0925-252000 Ext. 4206
Product areas 7, 8.
Contact Mr J. G. Tyror, Director of Safety.

Agfa-Gevaert Ltd
27 Great West Road, Brentford, Middlesex
TW8 9AX. Tel. 081-560 2131.
Product Areas 1.
Contact Miss Anne Sparrow.

American Medical Ltd
PO Box 971, London SW10.
Tel. 071-352 8051. Fax: 071-376 4508.
Product areas 1, 3, 4, 5, 7, 8.
Contact Betsy Riley, Managing Director.

Amersham International PLC
Lincoln Place, Green End, Aylesbury,
Bucks HP20 2TP. Tel. 0296 395222.
Product areas 4, 5, 6.
Contact Mr C. M. T. Medley, Sales and Marketing Manager.

Bard Ltd
Forest House, Brighton Road, Crawley,
West Sussex RH11 9BP.
Tel. 0293 527888, ext. 2204.
Product area 2.
Contact Peter Dekkers, Product Manager.

British Nuclear Fuels plc
Room 525, Hinton House, Risley,
Warrington, Cheshire WA3 6AS.
Tel. 0925 835022.
Product areas 8, 11.
Contact Dr R. J. Berry, Director of Health and Safety and Environmental Protection.

Bruel & Kjaer (UK) Ltd
92 Uxbridge Road, Harrow, Middlesex,
HA3 6BZ. Tel. 081-954 2366.
Product areas 3, 6.
Contatct Mr D. Lewis, Sales Manager.

Calumet Coach Co.
33 Shallbourne Rise, Camberley GU1J
2EJ. Tel. 0276 64490.
Product areas: 1, 4, 5.
Contact Mr P. Supple, Managing Director of International Operations.

Cardiac Services Ltd
95A Finaghy Road, South Belfast
BT10 OBY. Tel. 0232-625566.
Product areas 1, 3, 4, 5, 6.
Contact Mr R. J. Brown, Managing Director.

Cea (UK) Ltd
25 Presley Way, Crownhill,
Milton Keynes MK8 0ES
Tel. 0908 263090. Fax: 0908 263546.
Product areas 1, 3, 4, 5, 6.
Contact John Dunster, Managing Director.

Clinical Press Ltd
Redland Green Farm, Redland, Bristol BS8
7HF. Tel. 0272 420526.
Product area 17.
Contact Dr Paul Goddard, Chairman.

Computer General
5 Greenway Business Park, Bellinger
Close, Chippenham, Wiltshire SN15 1BN.
Tel. 0249 445566. Fax. 0249 445595.
Product areas 1, 10.
Contact Alan Mawdsely, Division Manager/Yvonne Morris, Marketing Manager.

Data-Med Computer Services Ltd
10 Faraday Building, Highfields Science
Park, University Boulevard, Nottingham
NG7 2QP.
Tel. 0602 431431. Fax: 0602 430782.
Product area 13.
Contact Mr C. Fildes, Sales Manager.

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610 Delta Office Park, Welton Road,
Swindon, SN5 7XF.
Tel. 0793 421771.
Product area 3.
Contact Geoff Faulkner, UK Manager.

Du Pont (UK) Ltd
Wedgwood Way, Stevenage, Hertfordshire SG1 4QN.
Tel. 0438 734000.
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Contact Mr E. G. Lovat, Product Manager, Diagnostic Imaging.

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Tel. 0753 855611.
Product areas 1, 6, 7, 8.
Contact Mr Roy Hauton, Sales Executive (Therapy).

Elscint (GB) Ltd
Colonial Business Park, Colonial Way,
Watford, Herts WD2 4PT. Tel. 0923 39511.
Product areas 1, 3, 4.
Contact Faith Gorman, Marketing Manager.

E-Z-EM Ltd
1230 High Road, Whetstone, London N20.
Tel. 081-446 9714.
Product areas 1, 2, 8.
Contact Richard Bayliss, Sales and Marketing Manager.

Fuji Photo Film (UK) Ltd
125 Finchley Road, London
NW3 6JH. Tel. 071-586 9351.
Product areas 1, 3.
Contact Mr R. G. Brown, Marketing and Administration Manager.

Gammex-RMI Ltd
34 Shakespeare Street, Nottingham
NG1 4FQ. Tel. 0602 483807.
Product areas 1, 3, 4, 5, 6.
Contact Mr Brian Scott, Commercial Manager.

IBM UK Laboratories Ltd
Scientific Centre, 2-5 St Clement Street,
Winchester, Hants, SO23 9DR.
Tel. 0962-844191.
Product areas 10, 13.
Contact Dr J.M. Knapman, Consultant Scientist.

IGE Medical Systems Ltd
352 Buckingham Avenue, Slough, Berks
SL1 4ER. Tel. 0753 874000.
Product areas 1, 2, 3, 4, 5, 6, 8, 9.
Contact Jill Mitchell, UK Sales Support.

Kodak Ltd
PO Box 66, Station Road, Hemel
Hempstead, Herts HP1 1JU.
Tel. 0442 61122.
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Contact Mr J. J. G. Tweed, Manager, Health Sciences Division.

Lanmark
PO Box 317, Beaconsfield, Bucks
HP9 2LR. Tel. 0494 791615/670586.
Product areas 1, 3, 4, 5, 9, 10, 15, 16.
Contact Liz Beckmann, Director.

3M UK PLC
3M House, Bracknell, PO Box 1,
Berks RG12 1JU. Tel. 0344 858000.
Product area 1.
Contact Mr Alan Budge, Marketing Manager.

Mallinckrodt Diagnostica (UK) Ltd
11 North Portway Close, Round Spinney,
Northampton NN3 4RQ. Tel. 0604-646132.
Product areas 4, 5.
Contact Mr D. G. L. Wood, Business Manager.

M. A. S. Medical Ltd
Armytage Road, Brighouse, West Yorkshire HD6 1QF. Tel. 0484 721906.
Contact Martin York, Managing Director.

Meadox (UK) Ltd
Matthew House, Matthew Street,
Dunstable LU6 1SD. Tel. 0582 605111.
Product area 2.
Contact Mrs Sheila Heap, Sales and Marketing Manager.

Medical Xray Supplies Ltd
Unit 12, Kingsbury Industrial Estate,
Church Lane, Kingsbury, London
NW9 8AU. Tel. 081-205 9500.
Product area 1.
Contact Mr R. J. Laird, Sales Director/Mr K. Wartnaby, Managing Director.

Mitsubishi Electric UK Ltd
Travellers Lane, Hatfield, Herts AL10 8XB.
Tel. 07072 78756.
Product area 14.
Contact T. F. McCloud, Sales and Marketing Manager.

Nuclear Associates
100 Voice Road, Carle Place, New York
11514-1593, USA. Tel. 516-741 7614.
Product areas 1, 3, 4, 5, 6, 8.
Contact Mr H. Glasser, General Manager.

Nucletron Trading Ltd
Nucletron House, Tarporley Business Centre, Tarporley, Cheshire, CW6 9UY.
Tel: 0829 733611.
Product areas 6, 8.
Contact Mrs Marilyn A. Hart, Office Manager.

Nycomed (UK) Ltd
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Sheldon, Birmingham B26 3EA.
Tel. 021-742 2444.
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Contact Mr L. Birch Hansen, Managing Director.

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Wharf Road, Eynsham, Oxford.
Tel. 0865 880880.
Product area 1.
Contact Pauline Hobday, Director of Sales and Marketing.

Philips Medical Systems
Kelvin House, 63–75 Glenthorne Road,
Hammersmith, London W6 OLJ.
Tel. 081-741 1666.
Product areas 1, 2, 3, 4, 6, 9.
Contact Mr R. Van der Ploeg, Marketing Manager.

Premise Engineering Ltd
Tibbs Hill Road, Abbots Langley,
Watford, Herts WD5 ODR.
Tel. 0923-267433/263320.
Product area 8.
Contact Mr R. K. Beach, Director.

Quantel Ltd
Administration Centre, Kiln Road,
Newbury, Berkshire RG13 2HA.
Tel. 0444 232323.
Product areas 2, 10.
Contact Mr C. Trim, Publicity Officer.

Radiological Protection Services Ltd
61 Lind Road, Sutton, Surrey SM1 4PP.
Tel. 081-643 6374.
Product area 8.
Contact B. H. Cutting, Managing Director.

Schering Health Care Ltd
The Brow, Burgess Hill, West Sussex
RH15 9NE. Tel. 0444 232323.
Product areas 1, 2, 3.
Contact Mr Simon Higginbotham or Mr S. Hearne, Product Managers.

Siemens plc
Siemens House, Windmill Road, Sunbury on Thames, Midlesex. Tel. 0932 752334.
Product areas: 1, 2, 3, 4, 6, 8, 9, 10, 13, 14, 15.
Contact L. J. McFadyen, Marketing Assistant.

Smith & Nephew Pharmaceuticals Ltd
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RM3 8SL.
Product area 1.
Contact Mrs Annette Drake, Sales Manager

Sony (UK) Ltd
Jays Close, Viables, Basingstoke, Hants
RG22 4SB. Tel. 0256 483564.
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Contact Richard Holt, Marketing Manager.

Toshiba Medical Systems UK
Manor Court, Manor Royal, Crawley, West Sussex RH10 2PY. Tel. 0293 560772.
Product areas 1, 2, 3, 4, 9, 10.
Contact Mr S. M. Weeden, Manager X-ray Products.

Toshiba Medical Systems Europe BV
Schieweg 1, 2627 An Delft, The Netherlands. Tel. 015 61 0121.
Product areas 1, 2, 3, 4, 9, 10.
Contact Mr P Blonk, Office Manager, X-ray BU.

Vertec Scientific Ltd
5 Comet House, Calleva Park Estate,
Aldermaston, Reading RG7 4QW.
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12: Quality assurance.
13. Radiology data management computer systems
14. Video printing
15. Equipment leasing
16. Hospital-shared services
17. Medical Publishing

Meetings and Courses

6th Asian Oceanian Congress of Radiology
December 14–18, 1991
New Delhi, India
Further details: M. L. Malhotra, Executive Secretary, Aggarwal Imaging Research Centre, 10-B, Kasturba Gandhi Marg, New Delhi 110 001, India.

Magnetic Resonance Basics at the University of Cambridge
December 15–20, 1991
Cambridge
Further details:Prof L D Hall, Herchel Smith Laboratory, University Forvie Site, Robinson Way, Cambridge CB2 2PZ. Fax: 0223-336748.

Mammographically Detected Early Breast Cancer
January 6–9, 1992
Naples, Florida
Further information: Dawne Ryals, Ryals and Associates, P.O. Box 1925, Roswell, Georgia 30077-1925, USA. Tel: (404) 641 9773. Fax: (404) 552 9859.

Non-ionising Radiation Protection
January 14, 1992
London
Further details: Dr D N S Dixon, Committee Secretary, The Society for Radiological Protection, 67 Oatlands Park, Linlithgow, West Lothian EH49 6AS.
Tel: 031-244 2779.

Abdominal Interventional Procedure
January 30–31, 1992
London
Further information: The Conference Office, Royal College of Radiologists, 38 Portland Place, London W1N 3DG. Tel: 071-636 4432. Fax: 071-323 3100.

MRI Teaching Course
January 30–31, 1992
Manchester
Further information: The Conference Office, Royal College of Radiologists, 38 Portland Place, London W1N 3DG.
Tel: 071-636 4432. Fax: 071-323 3100.

Radiation Dosimetry, Radiation Standards and Dosimetry Protocols
February 4–5, 1992
Teddington, Middlesex
Further details: Miss D H Pritchard, Building 62, Division of Radiation Science and Acoustics, National Physical Laboratory, Queens Road, Teddington, Middlesex, TW11 OLW. Tel: 081-943 6070 or 081-977 3222 ext 6070.

The Barts/London FRCR II Revision Course (MCQs, Film Reporting and Practice Vivas)
February 10-12, 1992
London
Further details: Mrs C Burrage, Course Secretary, Room 26, Dunn Laboratories, St Bartholowmew's Hospital, London EC1A 7BE. Tel: 071-601 7531.

Computed Body Tomography 1992 - The Cutting Edge
February 13-16, 1992
Florida, USA
Further details: Programme Coordinator, Johns Hopkins Medical Institutions, Office of Continuing Education, Turner Building, 720 Rutland Avenue, Baltimore, Maryland 21205. Tel: (301) 955-2959.

Head and Neck MRI at the University of L'Aquila
March 2-6, 1991
L'Aquila, Italy
Further details: Prof. R Passariello, Radiology, Ospedale SM Collemaggio, I067100, L'Aquila I, Italy. Fax: 39-682410997.

Skeletal Radiology Group of the Royal College of Radiologists
March 5-6, 1992
Coventry
Further details: Dr J Chandy, Consultant Radiologist, X-ray Department, Coventry & Warwickshire Hospital, Stoney Stanton Road, Coventry, CV1 4FH. Tel: 0203 224055.

Principles and Practice of Clinical MRI
March 5-8, 1992
Florida, USA
Further details: Programme Coordinator, Johns Hopkins Medical Institutions, Office of Continuing Education, Turner Building, 720 Rutland Avenue, Baltimore, Maryland 21205. Tel: 1 (301) 955-2959.

PET and SPECT Imaging of Living Brain Chemistry in Health and Disease
March 11–13, 1992
Maryland, USA
Further details: Program Coordinator, Johns Hopkins Medical Institutions, Office of Continuing Education, Turner Building, 720 Rutland Avenue, Baltimore, Maryland 21205, USA. Tel: 1 (301) 955-2959.

International Symposium on Recent Advances in Diagnostic Imaging and Radiation Oncology
March 24-27, 1992
Kathmandu, Nepal
Further details: Dr Naresh Prasad, Dept. of Radiology, Baylor College of Medicine, Houston, Texas 77030, USA. Tel: (713) 798 4415. Fax: (713) 798 5556.

24th International Diagnostic Course in Davos - ABDOMEN
March 28-April 3, 1992
Davos, Switzerland
Further details: IDKD, PO Box 224, CH-8028, Zurich, Switzerland. Tel: 01 262-2404.

The Biological and Epidemiological Basis for Radiation Protection Standards
April 1–2, 1992
Oxford
Further details: Dr D.N.S. Dixon, Programme Committee Secretary, The Society for Radiological Protection, 67 Oatlands Park, Linlithgow, West Lothian EH49 6AS. Tel: 031-244 2779.

6th Symposium Mammographicum
April 1-3, 1992
London
Further details: The Conference Office, The Royal College of Radiologists, 38 Portland Place, London, W1N 3DG. Tel: 071-636 4430. Fax: 071-323 3100.

Institute of Biology National Conference: Biology in Europe after 1992
April 2–3, 1992
Southampton
Further details: Andrea Silvester or Nicola Beaney, Institute of Biology, 20 Queensberry Place, London SW7 2DZ.
Tel: 071-581 8333.

Eurodop '92: Major International Symposium on the Medical Applications of the Doppler Effect in Diagnostic Ultrasound
April 5-8, 1992
Brighton
Further details: Eurodop '92, Bell Howe Conferences, 1 Willoughby Street, Beeston, Nottingham NG9 2LT. Tel: 0602 436323.

The Cambridge meeting on Chest Disease
March 25-27, 1992
Cambridge
Further details: Dr C D R Flower, Department of Diagnostic Radiology, Addenbrooke's Hospital, Hills Road, Cambridge CB2 2QQ. Tel: 0223 216203.

As a service to our readers, notices of meetings or courses will be inserted free of charge.
Please send articles for the Bulletin or any comments or suggestions you may have about the Bulletin to The Honorary Editor, BIR Bulletin, 36 Portland Place, London W1N 4AT.

Assurance of Quality in the Diagnostic X-Ray Department

The report of the BIR Diagnostic Methods Committee

Editors
J A Garrett, Director of Medical Equipment Management Organisation, Bristol & Weston Heath Authority, UK
D Gifford, Deputy Chief Physicist, Frenchay & Southmead Health Authorities, UK
M J Harvey, Middlesex Hospital, London, UK
P Goddard, Consultant Radiologist, Bristol Royal Infirmary, UK

Producing images, whether photographically or in electronic form, is the primary purpose of the diagnostic radiology department.

As the range of imaging modalities increases and the equipment for each becomes more sophisticated, awareness is growing of the necessity to review and assess the quality of the imaging process. While there are many interdependent factors that may affect image quality, each may in many cases be assessed by quite simple tests. As well as addressing the organisational, economic and human factors, which are a vital part of the imaging process, this handbook represents a wide range of well-tried tests suitable for use in both small and large X-ray departments.

The second section of the book presents the wider systems approach to quality assurance with reference to recent standards for QA and how these may be applied to diagnostic radiology.

The final part discusses quality assurance in computer assisted imaging, computed tomography, magnetic resonance imaging, and digital subtraction angiography.

Radiologists, radiographers, physicists and technicians alike will find *Assurance of Quality in the Diagnostic X-Ray Department* both a practical handbook for day-to-day use and a stimulus in developing their understanding of the scope of quality assurance.

November 1988 108 pages 296x208mm Spiralbound
0 905 74917 0 Illustrated £20.00

ORDER FORM

British Institute of Radiology, 36 Portland Place, London W1N 4AT.
Telephone Orders: 071 580 4189. Fax: 071 255 3209

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OPTIMIZATION OF IMAGE QUALITY AND PATIENT EXPOSURE IN DIAGNOSTIC RADIOLOGY

(BIR Report 20)

Editors:

B M Moores, B F Wall, H Eriskat and H Schibilla.

Contents: Introduction. Image Perception. Physical Assessment of Image Quality. Clinical Assessment of Image Quality. Optimization of Image Quality and Patient Dose - Paediatric Radiology - Mammography - Chest Radiography - Technical Factors. Patient Dose Measurements and Quality Assurance. CEC Image Quality and Exposure Criteria Trial. Panel Discussions. Conclusions and Perspectives for Future Research. CEC Study Group Document on Quality Criteria for Diagnostic Radiographic Images.

Key components in quality assurance in diagnostic radiology are image quality and patient exposure. Quality criteria defining optimum procedures should ensure that the most accurate and reproducible diagnostic information is obtained from radiographs, but at the same time minimize exposure of the patient to ionizing radiation. Formulation of such criteria was the aim of a workshop organized jointly by the CEC and NRPB, of which this book is the edited proceedings. A revised list of quality criteria for common diagnostic examinations was drawn up by a CEC Study Group and is appended to the proceedings.

October 1989 200 pages approx 266 x 196 mm
Softcover 0 905 74921 9 Illustrated £30.00

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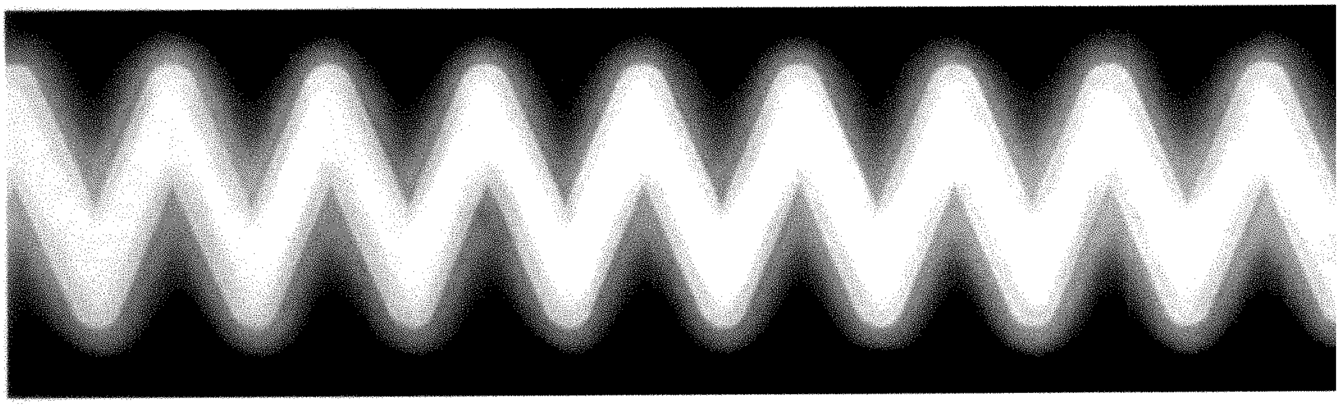

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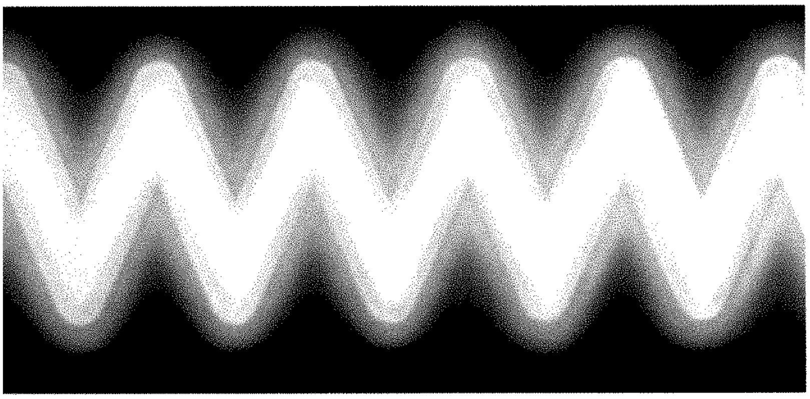

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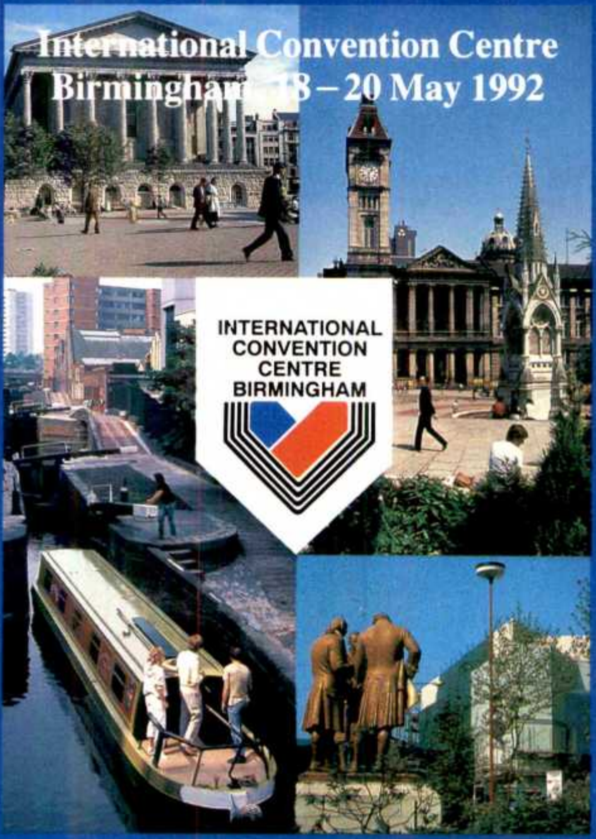
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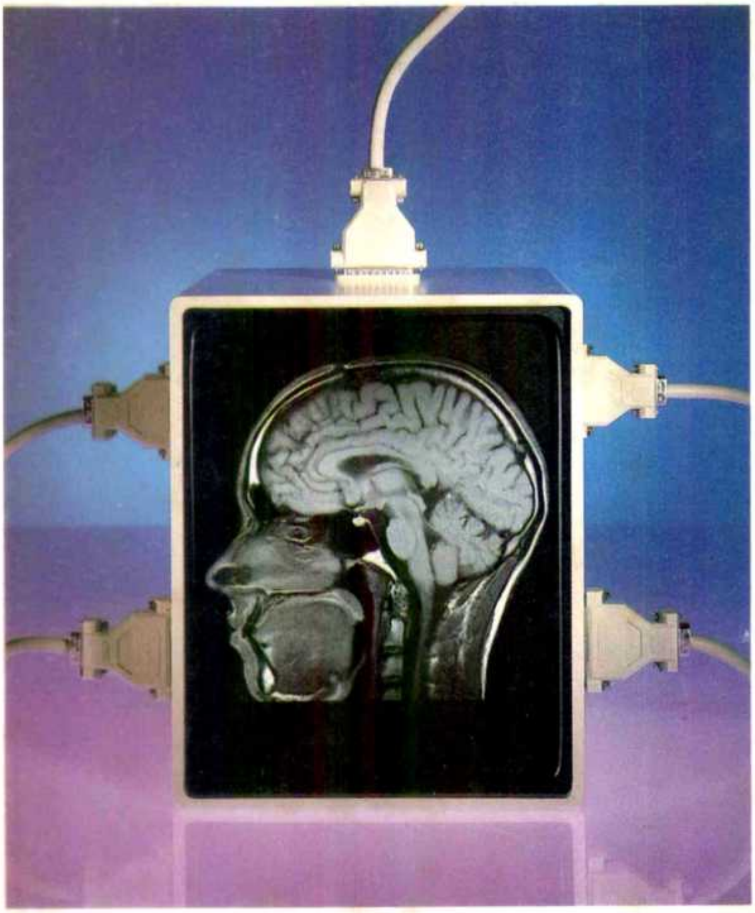

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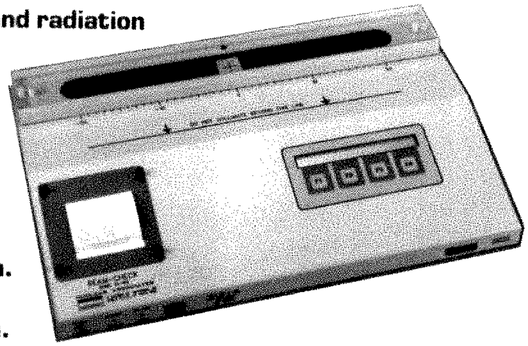

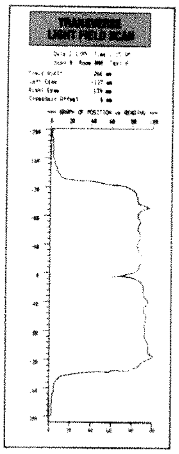

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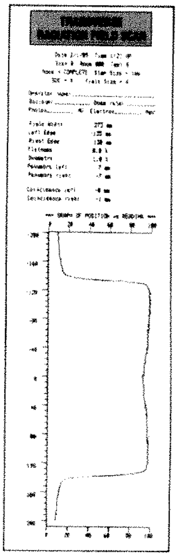

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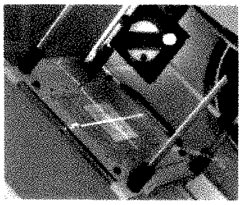

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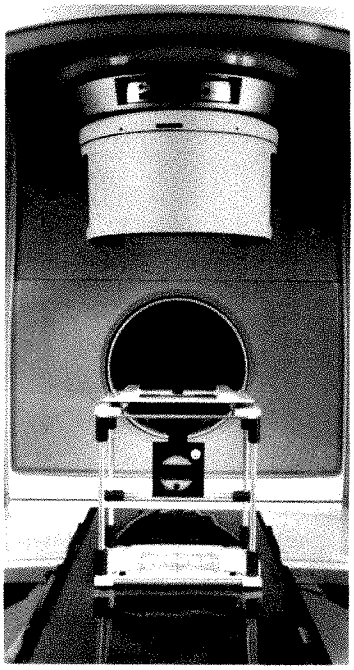

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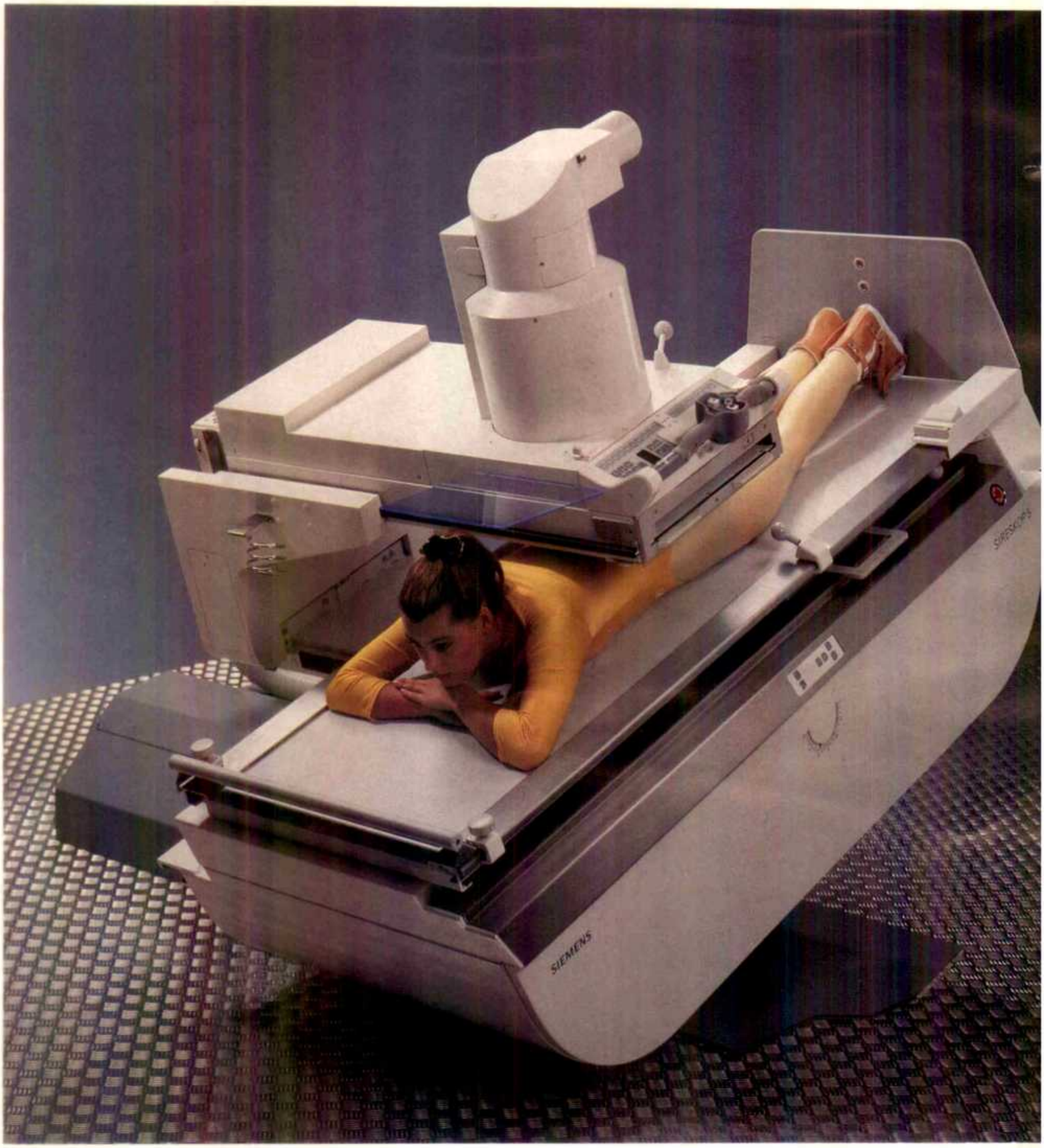

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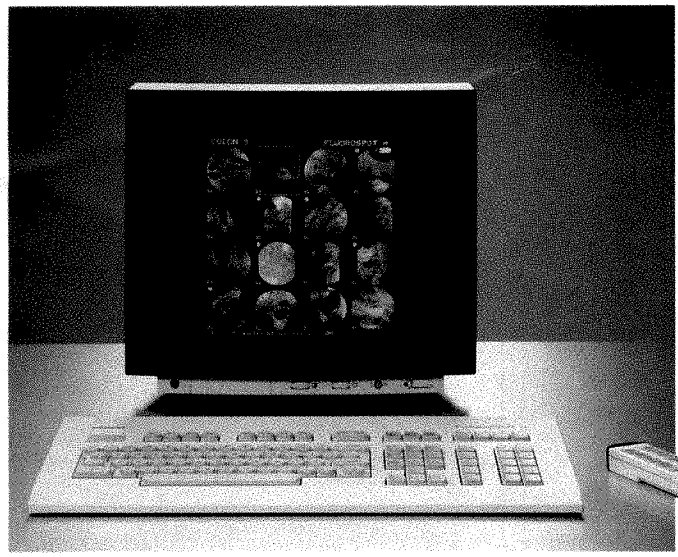

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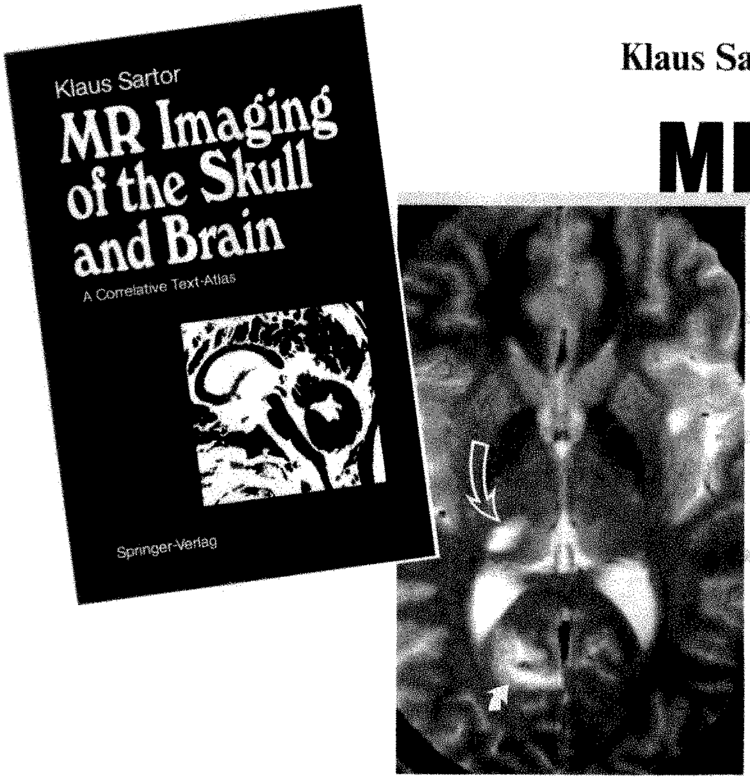

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The topic is treated by first giving a brief introduction on fundamental physics and chemistry; this is followed by a review of principles of examination and interpretation and normal functional anatomy. The major, clinical part of the book discusses the various disease categories entity by entity: developmental anomalies, mechanical trauma, tumors and related conditions, vascular diseases, infections and inflammations, demyelinating and degenerative diseases and miscellaneous conditions.

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The advantage of drawing on eight years of experience with MRI stands out clearly for readers of this clinically oriented, practical book.

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Review article

Striking a balance: benefit and risk in man's exposure to man-made radiations

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It is indeed an honour to be invited to give the Silvanus Thompson Memorial Lecture, and awesome when one considers the Hall of Fame represented by one's predecessors, starting with Lord Rutherford in 1918. Silvanus Thompson was the first President of the Roentgen Society, the forerunner of the BIR. Well ahead of his time, he would have today been labelled a "communicator". Born in York in 1851 he took his first degree in London in 1869 and returned to York as a Science Master. In 1876 he was appointed Professor of Experimental Physics in Bristol and in 1885 moved to the post of Principal Professor of Physics at the City and Guilds Technical College, Finsbury, which he held until his death in 1916. Elected a Fellow of the Royal Society in 1891, he followed his Presidency of the Roentgen Society in 1897, for the first year of its life, by the Presidency of the Institute of Electrical Engineers in 1899, the Physical Society in 1901 and the Optical Society in 1905. His was a key role in founding the multidisciplinary and broadly based organization that the British Institute of Radiology remains to this day.

Despite the euphoria that surrounded Roentgen's description of X rays, some of the risks of exposure to these novel radiations became apparent very early. The first publication of Roentgen's discovery in the English language in January 1896 was followed by the first description of "deterministic" effects only 3 months later. Writing in the *British Medical Journal*, Sydney Rowland cited a letter from Dr L. G. Stevens: ". . . workers on the new method often suffer from a variety of skin affections" (Rowland, 1896). The benefits, however, were easily seen. Military surgery depended largely on the removal of radio-opaque foreign bodies and it is of little surprise that an X-ray unit was in the field supporting the British forces on the North-West Frontier in 1897, at the Battle of Omdurman in 1898 and at sea by 1899 (Burrows, 1986).

Since my own move from London to Cheshire, I have become much more aware of the pioneering work in developing the use of X rays in medicine that was undertaken at Liverpool. Thurstan Holland, the scion of Liverpool radiology, was President of the Roentgen Society in 1904, and his Presidential address gives an intriguing insight into the balance of risk and benefit as seen by a leading practitioner of the time. "It is possible for anyone to rapidly master the technique of ordinary radiography. . . . whilst, with regard to the treatment of cases . . . it is comparatively easy to acquire enough information, so that at any rate one can use the X rays without the risk of doing any harm. . . . the keen delight which successful, early and first results brought; the intense excitement of the first coin seen stuck in an oesophagus, and easily and safely removed with a certain knowledge that it was there and to be removed; the scarcely less pleasure and excitement when a case of lupus was seen to yield to the X-ray treatment, when these successful cases could be counted on the fingers of one hand". He identified the areas of demonstrated value (Table I).

He went so far as to expostulate "the exploratory operation of cutting down on a kidney for 'suspected' stone ought to be . . . obsolete". However, he issued ". . . a word of warning against over-zeal. Some of us

Table I. Areas of demonstrated value of radiology (from Holland, 1904)

Surgical
Foreign body, especially war surgery
Injuries to bones and joints
Bone disease: TB and malignancy
"Bloodless method for reduction of congenital hip dislocation"
Renal stone

Medical
Chest disease:
  Tuberculosis
  Thoracic aneurysm

The Silvanus Thompson Memorial Lecture 1991, BIR Annual Congress, Brighton, April 1991.

are, perhaps, over confident as to the limitations of X-ray examination, and this over confidence will inevitably lead to mistakes and disappointment, and so tend to bring about distrust, not only in the lay mind but also in the minds of physicians and surgeons who do not themselves know very much about the details of X-ray work". He catalogued skin diseases that were treated successfully: acne, favus, ringworm, sycosis, eczema, psoriasis, removal of superfluous hairs, treatment of trachoma and ". . . most interesting . . . lupus, rodent ulcer and malignant disease other than rodent ulcer". Even in a time when science was largely respected by a curious public, he felt it necessary to issue a caution, ". . . it is a matter of common knowledge that the daily press has contained lately several somewhat sensational statements as to the dangers of X rays . . . calculated to do harm, as many of the general public reading them may be led to conclude that there is a danger of . . . cancer being caused by having an X-ray examination . . ." (Holland, 1904).

However, in the early days the most apparent dangers were to the practitioners, not the patients. The first death in the United Kingdom from accumulated radiation exposure occurred in 1902, followed by a steady and mournful procession until genuine public outcry followed the death of the Charing Cross Hospital's pioneer radiologist, Dr Ironside Bruce in 1921. This led to the setting up of the British X-Ray and Radium Protection Committee and ultimately to the setting up of the precursor to the International Commission on Radiological Protection (ICRP) by the Second International Congress of Radiology held in Stockholm in 1928 (Berry, 1986; Burrows, 1986).

Although textbooks of radiology carried warnings about the dangers attendant on the use of X rays, such as in Robert Knox's 1915 text, "The first care of all workers should be to ensure the complete protection of the operator and attendants in an X-ray department, and there can be no doubt that at present too little attention is paid in most electrical cliniques in this country to the important question of X-ray protection", and data were accumulating on measurable changes such as peripheral blood count depression in radium workers (Mottram, 1920), the first paper published in the English radiological literature commenting specifically on harm to patients was by Zweifel, a Munich radiologist in 1925. Under the title "The prevention of sickness after X-ray treatment", he pointed out that "the sickness is avoided by the use of a lead box encasing the tubes so constructed that no rays can escape to the patient except for the beam directed on the tumour . . . incidentally the doctor and nurse in the room are protected from scattered rays" — frank comment on the lack of perception of risk. 21 years before, Holland had advocated the Albers-Schoenberg method of field limitation of the X-ray beam when radiographing for renal stone to improve detail in the image! The benefits were, however, still seen to widely exceed the risks. Epilation for ringworm was a routine treatment until well into the 1930s; the risk of skin cancer induction following this treatment was only demonstrated many years later. The clear clinical usefulness of radiological methods led to an unwillingness to evaluate whether they carried associated risk. In the pre-antibiotic days, the management of tuberculosis by artificial pneumothorax showed clear value in improved rehabilitation. It was only many years later that the associated increased risk of breast cancer in females exposed to these repeated fluoroscopic examinations became apparent. Epidemiological studies showed not only the direct correlation of breast cancer risk with cumulative radiation exposure, but with statistically significant excess occurring at all doses above 1 Gy. Sensitivity to induction of breast cancer was also shown to depend on age at exposure, with a higher risk for those around the period of menarche (Boice & Monson, 1977).

However, the demonstration of an increased incidence of leukaemia in survivors of the Hiroshima/Nagasaki nuclear weapons detonations led to the setting up of comprehensive follow-up studies of this population, which has given us our largest quantitated evidence of delayed risks of radiation exposure to man. Most recent follow-up to over 40 years indicates an excess of some 300 cancers in a total population of about 100 000, with some 55% of all leukaemias in the population being radiation related, but only some 6% of other cancers. The data from the Hiroshima and Nagasaki survivors suggest that there are correlations between age at radiation exposure and cumulative lifetime risk of cancer development (Shimizu et al, 1988). These age–risk correlations differ for leukaemia and for solid cancers (Pierce et al, 1991), but although there is some evidence that irradiation at an early age does not result in a continuing excess cancer risk beyond 30 or 40 years, the overall risk of cancer development appears to be some two- to three-fold higher for those exposed as children. For particular cancers, the increase in risk per unit dose for those exposed under the age of 10 years may be up to 10-fold greater (although this estimate is based on small numbers of actual cases) and limited data on exposure *in utero* suggest similar risk values.

Following the observation of an early excess of acute leukaemias in the Hiroshima and Nagasaki survivors, interest was fired in the effect of occupational exposure of radiologists. The first of these studies used almost anecdotal methods and suggested that American radiologists had a nine-fold excess risk of dying of leukaemia when compared with other doctors (March, 1950). The first systematic epidemiological study of British radiologists was carried out by Professor Peter Smith and Sir Richard Doll and used as its subjects the 339 members of the British Institute of Radiology (BIR), who had joined this oldest radiological society in the world between 1897 and 1921 — the date at which the death of Ironside Bruce from chronic occupational radiation exposure led to a public outcry that made radiation protection a subject of concern amongst radiological practitioners. The study also included a further 999 members of the BIR who joined between 1921 and 1954 and followed their vital status to 1977. The occupational exposures received by the first cohort of 339 were dramatically higher than any subsequent group of radiation workers and this was associated with excess risk of leukaemia and of some of the other common cancers, but no excess of other causes of death. For the subsequent cohorts, for whom occupational radiation doses were lower, this excess risk of cancer induction decreased (Smith & Doll, 1981). A comparable study of American radiologists by the Johns Hopkins group appeared to show an excess of non-cancer deaths in the early radiologists; this was associated with a higher risk of infective disease, in particular tuberculosis, and also showed a decrease in risk as occupational exposures were reduced in the 1950s (Matanoski et al, 1975).

Recognition of the stochastic risk from radiation exposure, even in the absence of deterministic effects, led to the abandonment of many of the less justified uses of X rays. Radiation epilation for ringworm ceased totally. X-irradiation of the thymus ceased because its therapeutic usefulness was called into question, as well as because of the potential risk. Treatment of non-malignant skin conditions decreased, perhaps largely because of the availability of therapeutically effective alternatives such as topical steroids rather than because of an appreciation of the radiation risk. For other more serious conditions treated by radiotherapy, the balance of benefit and risk became more explicit. Doll and coworkers demonstrated the long-term risk of leukaemia, and later other cancer induction, in patients treated with radiotherapy for ankylosing spondylitis by whole-spine irradiation (Darby et al, 1987). Once again alternative treatment with steroids and cytotoxic drugs appears to have benefits for a large proportion of patients, but the use of radiotherapy, limited specifically to intractable joint pain, using the smallest possible radiation field, and having had prior discussion with the patient of the potential risks, may still be the treatment of choice. Long-term follow-up of over 100 000 women treated by intracavitary radium plus external radiotherapy for invasive carcinoma of the cervix has allowed the observation of the risk of induction of a second malignancy. After a small and transient increase in the risk of leukaemia, and overall, such women have a higher long-term risk of second malignancies than do women treated surgically. However, for some specific cancers the risk is actually *decreased.* There is a lesser risk of ovarian cancer for up to 15 years after therapy for carcinoma of the cervix, presumably owing to incidental radiation treatment to sub-clinical tumours; the disturbance to ovarian function caused by therapeutic radiation exposure is associated with a decreased risk of carcinoma of the breast, which lasts for up to 40 years (Boice et al, 1985).

But what of diagnostic uses of X rays? After the demonstration in the 1950s by Alice Stewart that a significant increase in childhood leukaemia was associated with obstetric radiography during the third trimester, confirmed by Mole in 1974, the use of this radiographic technique was restricted to those cases where the clinical problem was sufficiently severe to justify the risk, but was eventually supplanted by the advancement of ultrasound imaging. However, overall the use of diagnostic radiology has increased in the developed world and it represents the vast majority of annual exposure of the general population to man-made radiations (Fig. 1). Improvements in technology have allowed significant reductions in radiation dose to the patient and concomitant reduction in risk and at reasonable cost (Russell & Webb, 1985). However, a recent joint publication of the National Radiological Protection Board (NRPB) and Royal College of Radiologists has indicated that the standard of radiological practice varies widely throughout the UK and suggests that a significant number of diagnostic radiologists are unaware that their examinations may be a source of unnecessary risk to their patients. The NRPB identified four major causes of unnecessary X-ray exposure: those that were clinically unjustified (such as the routine pre-operative chest radiograph unless there is a high endemic tuberculosis risk); the repeat of radiographs recently taken elsewhere but unavailable; repeats of radiographs that have been rejected for technical reasons; and those examinations where the technique has not been optimized, and where the dose is not as low as reasonably achievable and there is need for improvement in either procedures or equipment.

In terms of reduction of risk, reduction of dose needs to be targeted to those examinations that contribute significantly to population exposure. Table II shows that only three examinations, representing some 6% of all radiographic studies, are responsible for nearly half the collective radiation dose, while studies that represent almost three-quarters of all X-ray examinations carried out are responsible for less than 5% of the collective radiation dose. Achieving significant reductions in risk requires targeting those examinations responsible for a significant proportion of population radiation exposure. Is it now time to ask whether the use of computed tomography (CT) is *ever* justified for imaging small children now that magnetic resonance imaging (MRI) is available? For adults, is it time to carry out a proper study of the cost-effectiveness of replacing X-ray examination of the lumbar spine by MRI? National surveys by the NRPB have demonstrated that for common examinations such as the barium enema, which *do* contribute significantly to collective radiation dose, there can be more than 10-fold variations in the radiation exposure for the same procedure carried out in different radiological departments. Table III shows the potential annual reduction in collective population dose in the UK in response to five actions that represent only good medical practice and good quality control in a radiological department. Surely it is not unreasonable to expect that a similar effort is devoted to quality control in reducing radiation doses to patients in X-ray departments as is expended in improving image quality.

A word in passing about non-medical uses of diagnostic X rays. In the 1940s and 1950s pedoscopes — X-ray fluoroscopic equipment — were widely used in

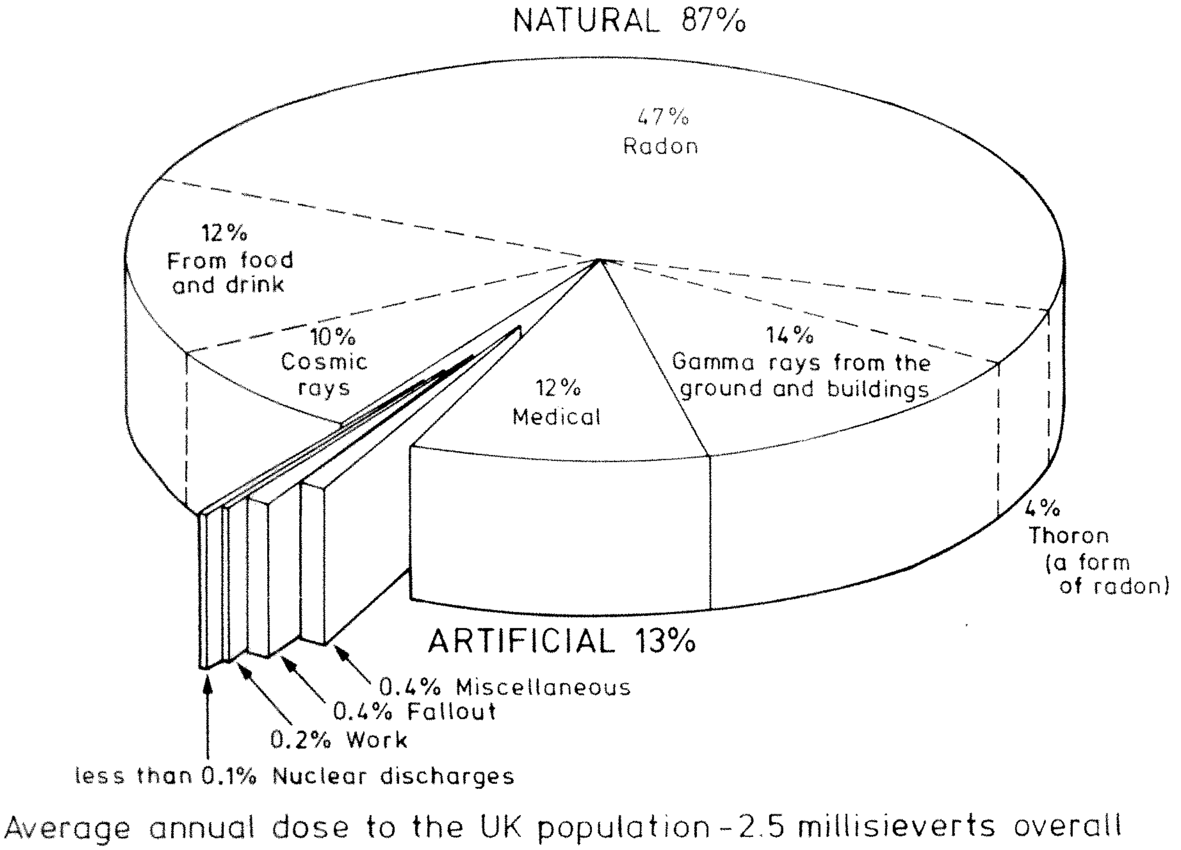

Figure 1. Distribution of sources of annual radiation dose to the UK population (Source: National Radiological Protection Board).

"better class" shoe shops. They provided a perfect solution to the problem of obtaining correctly sized shoes, but could expose the customer to doses in excess of 1 Gy to the foot, a dose rate of several mSv per hour to the whole body and even in excess of 1 mSv per hour throughout the whole shop. Their use was clearly not "justified", the first premise of the ICRP system of radiological protection, and has been banned for at least 30 years.

Table II. Diagnostic radiological examinations and their radiation dose consequences (from National Radiological Protection Board, 1990)

Examination	Frequency (%)	Collective dose (%)
CT	2.0	17
Lumbar/spine	3.3	15
Barium enema	0.9	14
Total	(6.2)	(46)
Chest	24	2.0
Limbs and joints	25	1.5
Dental	25	1.0
Total	(74)	(4.5)

Finally, despite my background in clinical medicine I am sure that in my present employment as guardian of Health and Safety and Environmental Protection for a major segment of the British nuclear industry you would

Table III. Potential annual collective dose saving as a function of improved radiological practice (From National Radiological Protection Board, 1990)

Method of dose reduction	Potential annual collective dose saving (man-Sv)
Eliminate clinically uphelpful examinations	3200
Reduce no. of films per examination to survey median value (SMV)	2500
Reduce fluoroscopy time to SMV	1500
Reduce hospital mean doses to survey third quartile value	1300
Reduce repeat rate from 10% to 5%	600
Total	9100

N.B. Annual collective dose to UK population from all occupational sources is 300 man-Sv and from nuclear power discharges is 30 man-Sv.

Table IV. Man-made disasters in the UK and abroad during the last 70 years

Location	Deaths	Cause
UK		
Senghenydd colliery (1921)	440	Electric circuit caused coal dust and methane explosion
Flixborough (1974)	28	Explosion following escape of gas from modified plant
Herald of Free Enterprise (1987)	184	Ferry capsized. Put to sea with vehicle doors open
Abroad		
Oppau, Germany (1921)	400	Ammonium nitrate 4500t exploded
Vaiont, Italy (1963)	2000	Hillside collapse into reservoir
Mexico City (1984)	> 500	Liquefied propane gas (LPG) explosion at refinery
Bhopal, India (1984)	2000	Methyl isocyanate released

expect me to comment on benefit and risk in the civil uses of nuclear energy. Table III indicates the potential annual collective dose saving from modest and achievable improvements in British radiological practice, which total some 9100 man-Sv per annum. By contrast, the collective dose received by the entire UK population from the discharges to the environment associated with the UK nuclear industry total only some 30 man-Sv. Figure 1 shows that the contribution made by the nuclear industry to the average annual radiation exposure to the population is frankly trivial, and well within the variation in natural background radiation that occurs even from one street to the next much less from one area to the next throughout the country. However, it is not the routine discharges of radioactive materials to the environment from the nuclear industry that dictate the unreasoning fear in which many people hold nuclear power. It is rather the risk of a catastrophic accident causing large numbers of deaths and widespread economic disruption.

Despite the public perception of the Chernobyl nuclear power plant accident as being the worst disaster ever suffered by mankind, it is not unique in terms of deaths caused or cumulative economic cost. Table IV outlines a few examples of UK and overseas man-made disasters of large consequences over the last 70 years. In the UK, the Health & Safety Executive has explored popular perceptions of risk from everyday activities and its discussion paper "Tolerability of Risk from Nuclear Power Stations" (1988) has suggested safety standards that the nuclear industry must achieve. Popular perception appears to regard a one-in-a-million risk as trivial, and a one-in-a-hundred chance of death as unacceptable regardless of the possible benefit. Within this compass, annual risks of deaths of 1 in 10 000 for a member of the general public and 1 in 1000 for workers in the industry are regarded as "tolerable". Popular perception is that employment in the nuclear industry is uniquely risky. This is not supported by the facts. Table V summarizes all acute fatal radiation accidents since 1945; a significant proportion are the result of accidents *not* in the nuclear industry. The health of workers employed in the nuclear industry has been carefully studied since the 1940s and to date has shown no significant excess of death from any cause and particularly from malignant disease consistently across all workforces studied. In fact all studies of nuclear workforces have tended to show the so-called "healthy worker effect" resulting from selection of fit individuals recruited to the industry and the benefits of relatively high socioeconomic status associated with employment in the industry (Beral et al, 1985; Smith & Douglas, 1986).

Occupational radiation exposures have been falling for many years so that it would be expected that risks would be greatest in those employed in the 1940s and 1950s. Two specific cohorts have been studied as potential bellwethers. One is the workers who were involved in fighting the fire that occurred in the Windscale No. 1 Military Pile in 1957, all of whom were exposed within the dose limits of the time. Another group is those workers whose cumulative occupational dose has exceeded 500 mSv. The data are shown in Figure 2. In neither of these groups is there a significant overall excess of mortality from any cause (Lawson et al, 1991). A recent report of a statistical association between preconception radiation exposure and the subsequent

Table V. Acute fatal radiation accidents (1945–1989)

	Number of events causing death	Acute deaths (radiation injuries)	Acute deaths (blast injuries)
Nuclear power production (Chernobyl)	1	29 + 11?	2
Criticality accidents (experimental facilities)	7	6	3
Industrial or medical accidents (sealed/external):			
within employer's premises	4 (2 in 1989)	4 employees	—
dispersed in public domain	5 (1 in 1987)	19 public	—

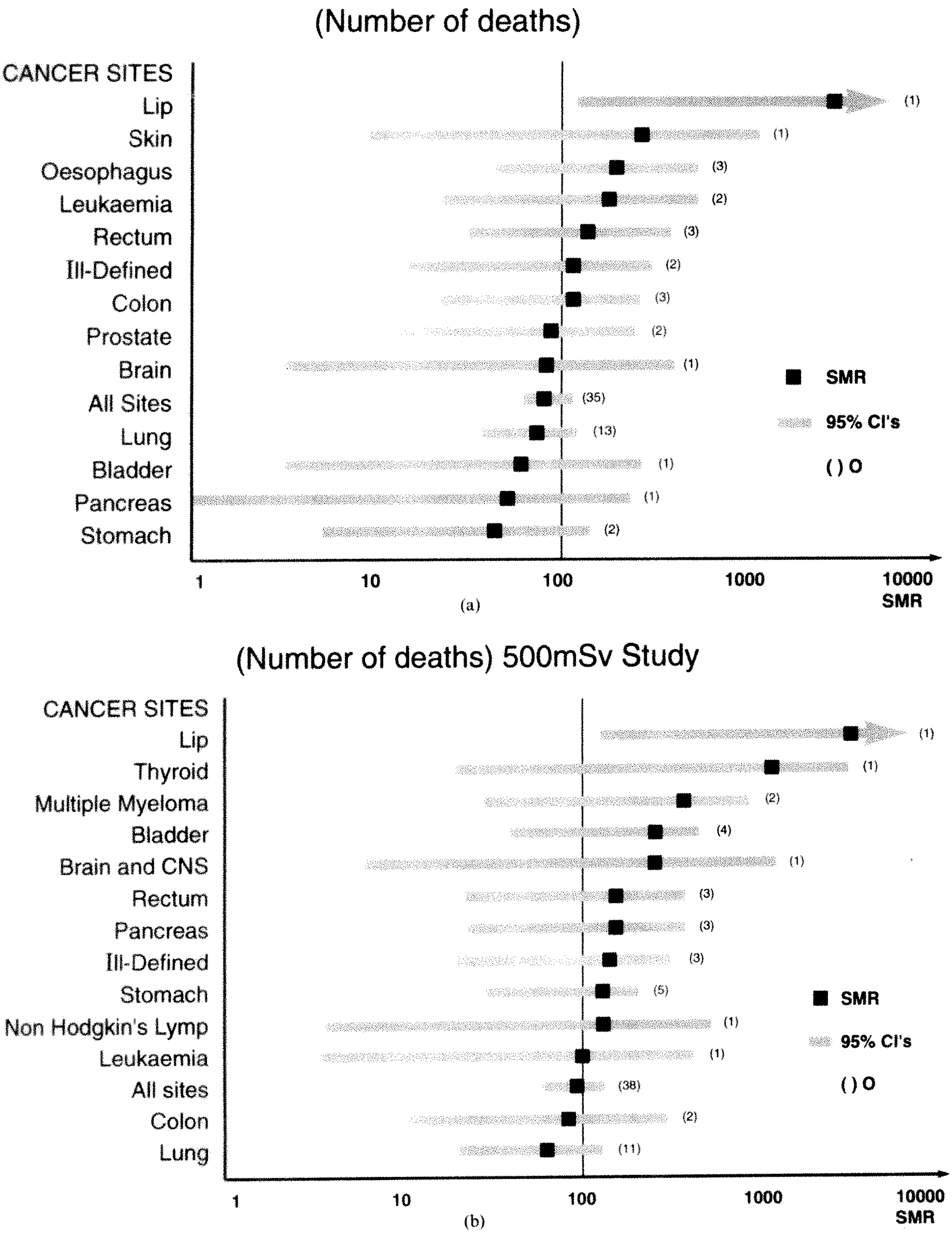

Figure 2. Standardized mortality ratios (SMR) and 95% confidence intervals for (a) 470 male employees known to have been involved in the 1957 Windscale fire or the subsequent clean-up operations, and (b) 542 employees identified by Smith and Douglas (1986) who had by the end of 1983 accumulated an external whole-body radiation exposure in excess of 500 mSv. Numbers in parentheses represent actual numbers of deaths (Lawson et al, 1991).

Table VI. Risk per gigawatt-year of energy (from Fremlin, 1989)

	Accidents		Operation	
	Work	Public	Work	Public
Hydroelectric	0.01–0.1	5	0.01–0.1	—
Wave power	1 ?	1	?	?
Coal/electric	1.0	0.01–0.1	0.6 ?	5
Oil/electric	0.25	0.1–0.2	0.05	5
Liquefied natural gas (LNG) and LPG	0.1–1	0.1–1	no data	
Nuclear/electric	0.01	0.01	0.03	0.01
Draught proofing	—	—	2–20	

development of leukaemia or lymphoma in Sellafield workers' children (Gardner et al, 1990) is not supported by evidence from children of the Hiroshima and Nagasaki atomic weapons survivors whose pre-conception radiation doses were even higher (Yoshimoto et al, 1991), or even by evidence from other UK nuclear sites (Urquhart et al, 1991).

But what are the benefits? All energy production is associated with risk, but the *absence* of energy is associated with a greater risk. Western society today has achieved greater longevity and absence of disease than any prior human society, and in the world today life expectancy is strongly correlated with average consumption of electric power per head. It is not unreasonable that developing countries should aspire to levels of comfort and longevity (and consumption of energy) similar to those now enjoyed in the developed West. The risks of power generation are shown in Table VI. By contrast, a medieval water mill (a *renewable* energy source, much in fashion today) would be associated with overall risk of deaths some 5000 times greater for a megawatt of energy converted (Fremlin, 1989). Even the conservation of energy is not without risk, and the operation of draught-proofing houses is associated with a risk per gigawatt of energy saved that is some 20 times or more the average risk of all forms of power generation and several hundred times the risk per gigawatt of electricity production from nuclear energy.

In summary, the risks of radiation to man are amongst the best understood and quantitated of present-day environmental hazards. Knowledge of radiation hazards to man is based soundly on over 90 years of actual experience of people thus exposed. For no other potential environmental hazard does such a comprehensive database exist. Radiological practice remains the single largest contributor to human exposure from man-made radiations. Its benefits are undoubted, but its risks deserve proper consideration and minimizing through the exercise of good clinical judgement and optimization of radiological technique. In his Presidential address to the Roentgen Society in 1897, Silvanus Thompson said "excepting only the introduction into surgery of Lord Lister's antiseptics and the discovery of anaesthetics, no discovery in the present century has done so much for operative surgery as this of the Roentgen rays". 94 years later, and with an almost unimaginably expanded horizon of clinical use, the balance remains strongly on the side of benefit.

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Percutaneous removal of retained intrahepatic stones with a pre-shaped angulated catheter: review of 96 patients

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Abstract. Intrahepatic biliary stone disease is prevalent in East Asia and there is a high frequency of retained intrahepatic stones after surgical treatment. Percutaneous removal of retained intrahepatic stones with a pre-shaped angulated catheter and a Dormier basket was attempted in a group of 96 patients who had a T-tube. Seventy-six had multiple intrahepatic stones, confined to one hepatic lobe in 52 patients. Stones were exclusively intrahepatic in 68 cases. Biliary strictures were present in 92 cases (95.8%). A combination of techniques was used including pre-shaped angulated catheters, irrigation suction, balloon dilatation of strictures, crushing of large stones and extracorporeal shockwave lithotripsy. Retained stones were completely removed in 48 cases, and incompletely removed in 22 cases. The overall success rate was 72.9%. There were only minor complications. No mortality or significant morbidity requiring hospitalization occurred. Angular deformity, stricture of bile ducts and impacted stones were the most frequent factors responsible for failure or incomplete removal of retained stones. Fluoroscopically guided percutaneous interventional procedures with a pre-shaped angulated catheter are useful complementary procedures to surgery for patients with intrahepatic stones. The major benefits of an individually angulated catheter are safety and easy access to small peripheral bile ducts.

Intrahepatic stones are frequently associated with recurrent cholangiohepatitis and complete surgical removal of the stones is often difficult because of the large number of stones and associated bile duct strictures (Wenn & Lee, 1972). Because a second operation for retained biliary stones results in a high mortality and morbidity, non-operative removal of the stones via a T-tube tract is widely used (Kerlan et al, 1985; van Sonnenberg et al, 1986; Choi et al, 1986; Park et al, 1987; Gandini et al, 1990).

While percutaneous removal of extrahepatic bile duct stones is relatively straightforward and excellent results have been reported (Burhenne, 1973, 1980), there have been few reports about the removal of retained intrahepatic stones (Choi et al, 1986; Park et al, 1987; Gandini et al, 1990). Removal of intrahepatic stones is more difficult than that of extrahepatic bile duct stones and requires a combination of techniques such as a pre-shaped angulated catheter and stone basket, and flexible choledochoscope sometimes combined with extracorporeal shockwave lithotripsy (ESWL) or intracorporeal electrohydraulic lithotripsy (Lear et al, 1984; Picus et al, 1989; Choi et al, 1991). While each technique has its own advantages and drawbacks, a pre-shaped angulated, individually selected catheter can negotiate the angulated or stenotic bile duct better than a comparably large choledochoscope.

In this study, we describe the results of treatment in 96 patients with retained intrahepatic stones using a pre-shaped catheter and a Dormier stone basket under fluoroscopic guidance.

Subjects and methods

Ninety-six patients with retained intrahepatic stones who had had previous biliary surgery and had a T-tube were treated from May 1986 to November 1990. Thirty-nine were men and 57 were women, ranging in age from 26 to 70 years with most of the patients in their 30s and 40s (mean age 45 years). Twenty patients had a single intrahepatic stone and most of the remainder more than five. Stones were confined to one lobe of the liver in 52 patients, both lobes in 44, and 28 patients had accompanying common duct stones (Table I).

At least 4 weeks after surgery, the T-tube was removed and a pre-shaped 9 F polyethylene tube and guide-wire with flexible tip was inserted through the T-tube tract. We had made several types of catheters beforehand to negotiate various angles of branching of the bile ducts and chose catheters according to the individual biliary anatomy of the patients (Fig. 1). Selective cholangiograms were obtained with a pre-shaped catheter to fill all ducts not demonstrated by conventional T-tube cholangiography owing to strictures or impacted stones. After thorough evaluation of the duct system and location of stones, the catheter was inserted into the peripheral duct beyond the stones. A Dormier basket was inserted through the catheter and expanded by withdrawing the catheter, and stones trapped and extracted by the basket. In severe strictures that impeded the passage of the catheter, ductoplasty was performed with a 6–10 mm angioplasty balloon catheter after instillation of 2% lidocaine into the bile

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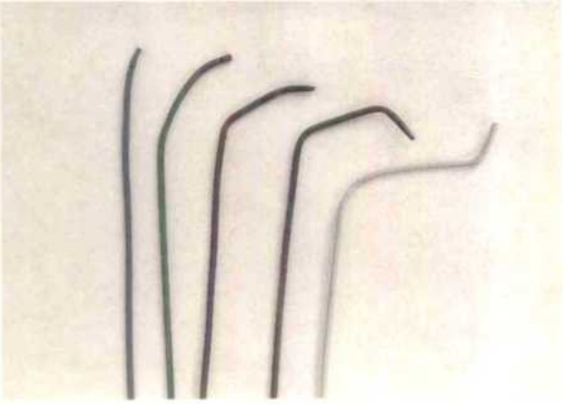


Figure 1. Pre-shaped catheters used frequently. If any did not fit the angle of the bile duct, a new catheter was made according to the anatomy of the bile duct.

ducts. Other techniques used were crushing of the stone by a mechanical lithotriptor basket (Medi-tech, Massachusetts, USA) or snare, or irrigation suction by a large bore tube (12–20 F Nelaton rubber tube with multiple side-holes), occlusion balloon or Fogarty catheter (Kaufman et al, 1979; Kerlan et al, 1985; van Sonnenberg et al, 1986; Park et al, 1987). In cases of severe or anticipated difficulty in a conventional interventional procedure, ESWL was performed with an EDAP LT01 Piezoelectric lithotriptor (17 cases). Details of our ESWL procedures have been described previously (Choi et al, 1991).

Table I. Number and location of intrahepatic stones

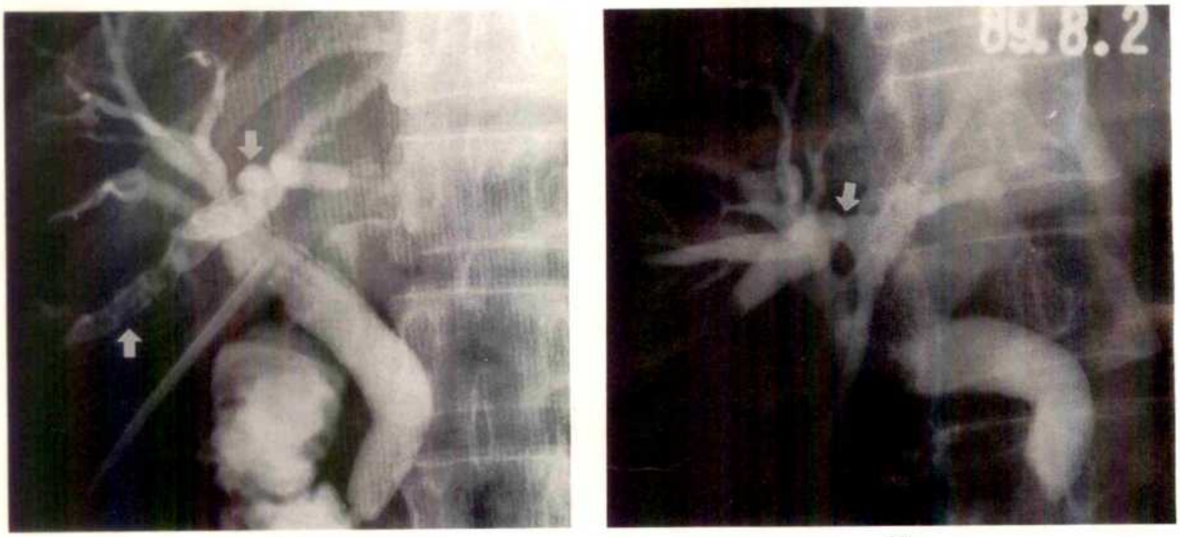
Right duct	Left duct			
	(—)	Single	Multiple	Total
(—)	—	18	8	26
Single	2	1	1	4
Multiple	24	41	1	66
Total	26	60	10	96

All procedures were performed on an outpatient basis. All patients received oral broad-spectrum antibiotics (ampicillin 2 g per day) for 3 days after the procedure. During each procedure, pethidine (50 mg) was given intramuscularly. No procedure was longer than 90 min. If we could not remove all stones in a single session, the procedure was repeated after 1 week.

Success was considered complete if all retained stones were removed, and as incompletely successful if more than two-thirds of the retained stones were removed and there was no evidence of obstructive jaundice.

Results

In 92 cases (95.8%), strictures of the bile ducts were noted. Strictures were in the left hepatic lobe in 34 cases, in the right lobe in 23 cases and in both lobes in 34 cases (Table II). In 27 cases, balloon dilatation was performed to facilitate the passage of a catheter or stone fragments. A 12–16 F Nelaton rubber tube was inserted through



(a)

(b)

Figure 2. (a) Multiple retained stones are noted in the posterior inferior division of the right intrahepatic bile duct, which originates from the left hepatic duct (arrow). (b) Selective cholangiogram obtained in the right anterior oblique view demonstrates the acute branching angle of the duct (arrow), which was successfully negotiated by a pre-shaped 9 F polyethylene catheter. All retained stones were successfully removed.

Table II. Location of strictures in intrahepatic ducts

Right duct	Left duct		
	(−)	(+)	Total
(−)	4	34	38
(+)	23	34	57
Total	27	68	95*

*One case had a stricture at the choledochojejunostomy site.

the narrow segment of the bile duct and kept there for at least 4 weeks to prevent re-stenosis.

The average number of sessions required was 3.7 ± 2.9 and ranged from 1 to 22. In 48 cases (50%), all retained stones were removed (Fig. 2) and incomplete success was achieved in 22 cases (Fig. 3). The overall success rate was 72.9%. The success rate of removal of left hepatic duct stones was higher than that of right duct stones; however, the difference was not statistically significant (84.6% vs. 61.5%, $p = 0.063$) (Table III). Removal of associated extrahepatic duct stones was uniformly successful. Removed stone fragments were black or dark brown, suggestive of bile pigment in all patients.

The most frequent causes that led to incomplete success or failure were acute angulation deformities and strictures of the bile ducts and impacted stones that hindered either passage of a catheter or expansion of the stone basket (Table IV, Fig. 4).

Right upper quadrant pain, nausea and vomiting occurred not infrequently during the procedure. Minor haemobilia was frequently associated with balloon dilatation of duct strictures. These minor complications were treated by observation alone or analgesics. Fever and chills caused by associated infection were controlled with oral antibiotics and subsided in 2–3 days. When the T-tube tract was damaged by the procedure, observation for 1–2 weeks before another attempt was sufficient. There was no significant morbidity leading to hospitalization or mortality in our series.

Discussion

The incidence of intrahepatic stone disease (also known as Oriental cholangiohepatitis, recurrent pyogenic cholangitis) in Western countries is low (Federle et al, 1982). However, this disease is common in Asia (9–17% in Korea, 4–10% in Japan, 15% in Hong Kong, and 35% in Taiwan) (Choi et al, 1986; Park et al, 1987). Although the exact cause is not known, it is postulated that portal bacteraemia, metabolic derangement caused by low socioeconomic status, poor hygiene and dietary insufficiency result in cholangitis and stone formation. In some countries, infestation by *Clonorchis sinensis* or *Ascaris lumbricoides* may play some role (Wenn & Lee, 1972; Wastie & Cunningham, 1973).

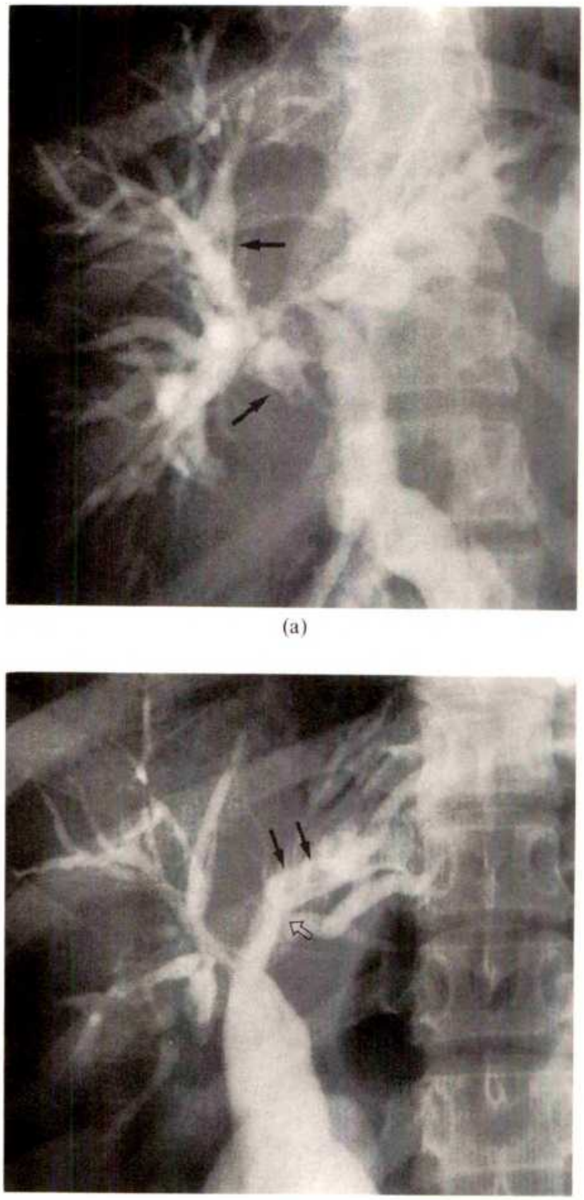

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Figure 3. (a) Selective cholangiogram obtained at the orifice of the stenotic right intrahepatic duct shows multiple retained stones (arrows). (b) After balloon dilatation of the stenotic right duct orifice, right intrahepatic stones were successfully removed. Two left intrahepatic stones (black arrows) in a short segmental duct with a narrow orifice (open arrow) could not be removed because the basket did not expand. This case was classified as an incomplete success.

Cholecystectomy, intrahepatic stone extraction and biliary drainage procedures such as choledochojejunostomy are usually performed but are not successful in removing all the intrahepatic stones except after left lateral segmentectomy or lobectomy in localized disease

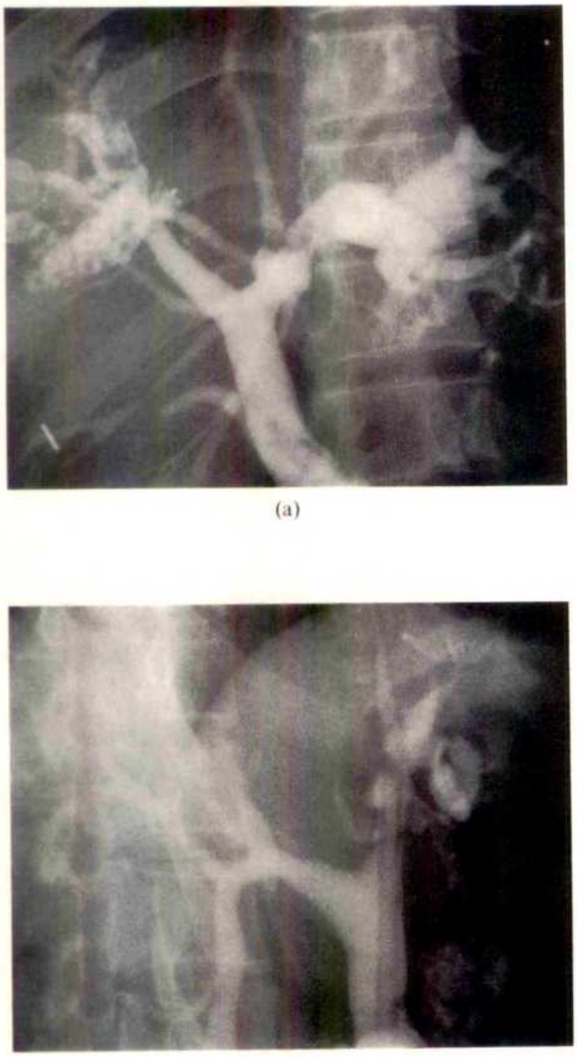
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Figure 4. Causes of failure or incomplete removal. (a) Conventional T-tubogram shows multiple impacted stones in the right intrahepatic duct. Because of severe impaction and stricture, a balloon catheter could not be passed. (b) Because of steep angulation of the bile duct and stenosis of the orifice, the catheter could not enter the duct.

Table IV. Causes of failure to remove all stones

	Failure	Incomplete success
Angulation	14	8
Stricture	11	10
Impaction	10	4
Large stone	0	3
Tortuous tract	1	0
Short segment	1	0
Too many stones	1	0
Refused follow-up	3	3
Total*	41	28

*Some cases had more than one cause.

in a small number of patients. Surgical cure rate is thus very low, reported as 13.3% (Wenn & Lee, 1972).

Since the frequency of retained intrahepatic stones is high and mortality and morbidity rates are higher for a second operation, non-surgical percutaneous removal is the appropriate management for these patients. There are several alternatives to surgical re-operation for retained intrahepatic stones, such as percutaneous removal through a T-tube tract under fluoroscopic or choledochoscopic guidance, laser lithotripsy or direct electrohydraulic lithotripsy (Choi et al, 1986; Park et al, 1987; Gandini et al, 1990). Choi et al (1986) reported a completely successful removal in 51 of 62 intrahepatic duct stone patients with a flexible choledochoscope and basket removal (success rate 82.3%). Their high success rate was attained by repeated endoscopic sessions through a hepatico-cutaneous-jejunostomy with balloon dilatation. Combination of their technique with extra- or intracorporeal shockwave lithotripsy may increase the success rate (Gandini et al, 1990). Our series included a higher proportion of patients with biliary strictures (95.8% against 22.3%) and angular deformity of the bile ducts so that even negotiation of the duct with a 9 F pre-shaped angulated, individually selected catheter was impossible. This factor may be responsible for the difference of success rate.

There has been a minor improvement of success rate since our previous report by Park et al (1987): complete

Table III. Success rate of percutaneous removal of retained intrahepatic stones

Location	Total number	Complete success	Incomplete success	Failure	Success rate (%)
Right	26	15	1	10	61.5
Left	26	19	3	4	84.6
Both	44	14	18	12	72.7
Total	96	48	22	26	72.9

success 48.6% and incomplete success 18.9%. This minor improvement is probably attained by the recent use of ESWL, with which 10 and four patients out of 17 cases with problems in conventional treatment were completely or incompletely successfully treated, respectively. The impact of ESWL in treating retained intrahepatic stones has been discussed previously (Choi et al, 1991).

Our percutaneous removal technique with the use of a pre-shaped angulated catheter through a T-tube tract under fluoroscopic guidance has advantages over the choledochoscopic method in that individually selected catheters can negotiate acute angles in the biliary tree and approach stones in small peripheral ducts, additional expensive devices are not needed, and there are less complications. However, the high radiation exposure to the patient and the hand of the operator is a disadvantage.

Combining all available modalities in each individual case is recommended to achieve better results. Despite multiple sessions and many techniques, our results are not so far satisfactory. More efficient and safe crushing methods such as intracorporeal shockwave lithotripsy with a flexible tip on a pre-shaped catheter under fluoroscopic guidance can be expected in the future.

In summary, percutaneous removal of retained intrahepatic stones with a pre-shaped catheter is a safe method and at least partially effective in 72.9% of our series. Severe angular deformities and strictures of the bile ducts and large impacted stones were the factors responsible for our failures.

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Tumour and tumour-like conditions of the soft tissue: magnetic resonance imaging features differentiating benign from malignant masses

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Abstract. 49 primary soft-tissue masses were studied by magnetic resonance imaging (MRI) in an effort to differentiate benign from malignant lesions. There were 24 benign and 25 malignant tumours. Images were evaluated for the presence of low-signal septation, changes in pattern of homogeneity, signal intensity, and margin definition and shape. 20 of the 25 malignant tumours (80%) demonstrated low-signal septation, and two of the 24 benign tumours (8%) also demonstrated this feature. Malignant tumours tended to change pattern from being homogeneous on T_1-weighted images to being heterogeneous on T_2-weighted images (72%). Benign tumours maintained their pattern on both sequences (67%). Only three of the 24 benign tumours (12.5%) changed from being homogeneous to heterogeneous. Our findings suggest that tumours which change pattern, from homogeneous on T_1-weighted images to heterogeneous on T_2-weighted images, and tumours which have low-signal septations are likely to be malignant. Moreover benign lesions tend to have well defined margins, and some benign masses have characteristic appearances that aid in their differentiation from malignant processes.

Since the introduction of magnetic resonance imaging (MRI), its diagnostic efficacy has been compared with computed tomography (CT). While the superiority of MRI for visualizing the skeleton and surrounding soft tissues has been documented (Petasnick et al, 1986; Totty et al, 1986; Demas et al, 1988; Sundaram et al, 1988; Kransdorf et al, 1989a; Berquist et al, 1990), its ability to provide a histological diagnosis has not been established.

There are no established features with which to predict or distinguish malignant from benign lesions, although tumour signal intensity, margination, homogeneity and the presence of calcification have been used by some authors (Totty et al, 1986; Sundaram et al, 1988; Kransdorf et al, 1989a; Berquist et al, 1990). By modifying these criteria to include tumour morphology, presence of septation, changes in pattern of homogeneity, signal intensity and margin definition, we have attempted to identify certain trends that may be useful in distinguishing benign from malignant tumours.

Materials and methods

MR images of 49 primary soft-tissue masses in 49 patients were reviewed. The patients, 26 males and 23 females, ranged in age from 6 to 75 years. The overall average age of the patients was 42 years in the benign and 38 years in the malignant groups.

In most cases, the MRI studies were performed in our institution, but in several instances the patients were referred to us for second opinions or for surgery. All patients underwent surgery at our institution.

The MRI scans were obtained on an Elscint 5000 0.5 T, Siemens Magnetom 1.0 T or a Diasonic 0.3 T system, but we did not evaluate images for possible differences in field strength. Multisection and multiplanar techniques were applied in the majority of cases. Spin–echo T_1- and T_2-weighted pulse sequences were 450–700/20–30 TR/TE (repetition time/echo time) and 1800–2200/80 TR/TE, respectively. The images were obtained in a combination of coronal, sagittal and/or axial planes. Section thickness varied from 4 to 10 mm. Surface coils were used appropriate to the site being imaged. In all cases diagnosis was confirmed with the pathological specimen except in three cases in which a radiological diagnosis could be made with certainty (*e.g.* two small lipomas and one popliteal cyst), obviating the need for operation.

The MR images were reviewed by two radiologists together (G.H. and T.T.M.) and were evaluated with regard to: (1) shape, (2) morphology, (3) pattern, (4) signal intensity, and (5) definition of margins. The shape of the tumour was considered either round–oval or irregular. Morphology refers to the presence of low-signal septations which traversed the lesion and divided

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it into lobules. Tumours could demonstrate low-signal septations while maintaining an overall shape of round–oval, but an external contour of lobulation was not possible without septation, and such a shape by definition was irregular. The pattern was described either as homogeneous if all sections had uniform signal, or heterogeneous if the lesion contained varied signal. Any change in pattern between T_1-weighted images (T_1-WI) and T_2-weighted images (T_2-WI) was noted. The evaluation of signal intensity was based on comparison with adjacent muscles in both T_1-WI and T_2-WI and was graded as low, equal or high. Tumour margins were evaluated as ill defined, partially or well defined according to their relationship to the surrounding tissue: ill defined when the borders were confluent with the surrounding tissue; partially defined if at least part of the border of the mass was confluent with the surrounding tissue; and well defined when the entire tumour was sharply demarcated from the adjacent tissues.

Results

Of the 49 soft-tissue masses, 24 were benign and 25 malignant (Tables I, II).

In the benign group, eight occurred in the thigh, four in the pelvis, three in the shoulder region, three in the calf, two in the forearm, two in the popliteal fossa, one in the ankle and one in the foot.

In the malignant group, 10 occurred in the thigh, four in the popliteal fossa, three in the calf, three in the back, two in the foot, two in the elbow, and one in the hip (Fig. 1). The size of the tumours ranged from 2 to 20 cm, with an average of 8 cm in greatest diameter.

Shape and morphology

The overall configurations of the mass in both benign and malignant lesions were equally divided. 27 were round–oval (14 malignant, 13 benign) and 22 irregular (11 malignant, 11 benign). Low-signal septation was present in 20 of 25 malignant lesions (80%) (Fig. 2) and in only two of 24 benign masses (8%). 18 of the 20 (90%) malignant septated masses can be broadly classified histologically as spindle cell tumours: 10 malignant fibrous histiocytomas, three synovial sarcomas, one malignant Schwannoma, one undifferentiated spindle cell sarcoma, one liposarcoma, one haemangiopericytoma and one extraosseous osteosarcoma. The remaining two septated malignancies were extraosseous

Table I. Benign conditions ($n = 24$)

Tumour	T_1-WI			T_2-WI			Septation
	Pattern	SI	Definition	Pattern	SI	Definition	
Lipoma	Hm	+	+ + +	Hm	+	+ + +	–
Lipoma	Ht	+	+ + +	Ht	+	+ +	–
Lipoma	Hm	+	+ + +	Hm	+	+ + +	–
Lipoma	Hm	+	+ + +	Hm	+	+ + +	–
Lipoma	Hm	+	+ + +	Hm	+	+ + +	–
Atypical lipoma	Hm	+	+ +	Hm	+	+ + +	+
Neurofibroma	Ht	=	+ + +	Ht	+	+ + +	–
Neurofibroma	Hm	+	+ + +	Hm	+	+ + +	–
Neurofibroma	Ht	+	+ + +	Hm	+	+ + +	–
PVNS	Hm	=	+ + +	Ht	=	+ + +	–
PVNS	Ht	=	+	Ht	=	+	–
Ganglion	Ht	–	+ +	Hm	+	+ + +	–
Ganglion	Hm	–	+ + +	Ht	+	+ + +	–
Desmoid	Ht	=	+ + +	Ht	+	+ + +	–
Desmoid	Hm	–	+ +	Hm	–	+ +	–
Haematoma	Ht	+	+ + +	Ht	+	+ +	–
Haematoma	Ht	+	+ +	Ht	+	+ +	–
Abscess	Ht	+	+ + +	Hm	+	+ + +	–
Abscess	Ht	+	+ + +	Hm	+	+ + +	–
Infection	Ht	=	+	Hm	+	+ + +	+
Popliteal cyst	Ht	+	+ + +	Hm	+	+	–
Myxoma	Hm	–	+ + +	Ht	+	+ + +	–
Haemangioma	Ht	+	+ + +	Hm	+	+ + +	–
Benign Schwannoma	Hm	=	+ + +	Ht	+	+ + +	–

Pattern: Hm, homogeneous; Ht, heterogeneous.
SI: (–) SI less than adjacent muscle, (=) SI equal to adjacent muscle, (+) SI greater than adjacent muscle.
Definition: (+) poorly defined margins, (+ +) partially well defined, (+ + +) well defined.
Septation: (–) none, (±) seen on T_2-WI only, (+) present on T_1- and T_2-WI.

Ewing's sarcoma and an alveolar soft-part sarcoma. The two benign septated masses consisted of an abscess and an atypical lipoma. None of the benign spindle cell tumours (*e.g.* neurofibroma, benign Schwannoma, desmoid) showed any evidence of septation.

Pattern

In the malignant group, 18 of the 25 tumours (72%) changed pattern between T_1- and T_2-WI: 16 changed from homogeneous to heterogeneous (Fig. 3) and two vice versa. Seven of 25 (28%) did not change pattern: one remained homogeneous and six remained heterogeneous. In contrast, only eight of the 24 benign tumours (33%) changed pattern (three homogeneous to heterogeneous and five vice versa). Sixteen of the 24 benign tumours (67%) did not change, with eight remaining homogeneous and eight heterogeneous on both sequences.

Combining the two groups, 26 of the 49 masses changed pattern, and eighteen of the 26 (69%) were malignant. More significantly, 19 of these 26 changed from a homogeneous pattern on T_1-WI to a heterogeneous one on T_2-WI, of which 16 (84%) were malignant. The remaining seven of 26 tumours changed from heterogeneous to homogeneous, of which only two (29%) were malignant and five (71%) were benign.

In contrast, 23 of the 49 masses did not change pattern. Of these 23 masses, 16 (70%) were benign. Nine tumours remained homogeneous, of which eight (89%) were benign. 14 tumours remained heterogeneous: eight benign (57%) and six malignant (43%).

Signal intensity

Compared with adjacent muscle on T_1-WI, 10 of 25 malignant tumours showed a high signal, one a low signal and 14 of 25 as isointense signal. However, all these tumours showed high signal on T_2-WI. Overall, 15 of 25 (60%) changed signal intensity.

The benign tumours had high signal intensity in 14 of 24 lesions on T_1-WI, isointensity in six and low signal intensity in four. 21 of the 24 exhibited high signal on T_2-WI. The three benign tumours that were not intense on T_2-WI included two pigmented villonodular synovitis (PVNS), which were isointense on both T_1- and T_2-WI, and one desmoid tumour which was of low signal intensity on both. Overall, only seven of 24 (29%) changed signal intensity. Combining the results, 18 tumours were isointense on T_1-WI and bright on T_2-WI, of which 14 (78%) were malignant.

Margin definition

10 malignant lesions were well defined, 10 were partially defined and one poorly defined on both T_1- and T_2-WI. In addition, two changed from partially to well

Table II. Malignancies ($n = 25$)

Tumour	T_1-WI			T_2-WI			Septation
	Pattern	SI	Definition	Pattern	SI	Definition	
MFH	Ht	=	+	Hm	+	+	–
MFH	Hm	=	+ + +	Ht	+	+ + +	±
MFH	Hm	=	+ + +	Ht	+	+ + +	+
MFH	Hm	=	+ + +	Ht	+	+ + +	+
MFH	Hm	+	+ +	Ht	+	+ +	±
MFH	Hm	=	+ + +	Ht	+	+ + +	+
MFH	Hm	+	+ + +	Ht	+	+ + +	+
MFH	Hm	=	+ +	Ht	+	+ + +	+
MFH	Hm	+	+ +	Ht	+	+ +	+
MFH	Hm	=	+ + +	Ht	+	+ +	±
MFH	Ht	=	+ +	Hm	+	+ + +	–
MFH	Ht	+	+ + +	Ht	+	+ + +	±
Synovial sarcoma	Hm	+	+ +	Ht	+	+ +	±
Synovial sarcoma	Hm	+	+ + +	Ht	+	+ + +	+
Synovial sarcoma	Hm	–	+ +	Ht	+	+ +	+
Malignant Schwannoma	Ht	=	+ + +	Ht	+	+ + +	–
Malignant Schwannoma	Hm	+	+ +	Ht	+	+ +	+
Extraosseous Ewing's sarcoma	Hm	=	+ +	Ht	+	+ +	±
Extraosseous Ewing's sarcoma	Hm	=	+ + +	Ht	+	+ + +	–
Spindle cell sarcoma	Ht	+	+ +	Ht	+	+ +	+
Liposarcoma	Ht	+	+ + +	Ht	+	+ + +	+
Extraosseous osteosarcoma	Ht	=	+ +	Ht	+	+ +	+
Lymphoma	Hm	=	+	Ht	+	+ + +	–
Haemangiopericytoma	Hm	=	+ +	Hm	+	+ +	+
Alveolar soft-part sarcoma	Ht	+	+ +	Ht	+	+ +	±

MFH = Malignant fibrous histiocytoma. See Table I for key to symbols.

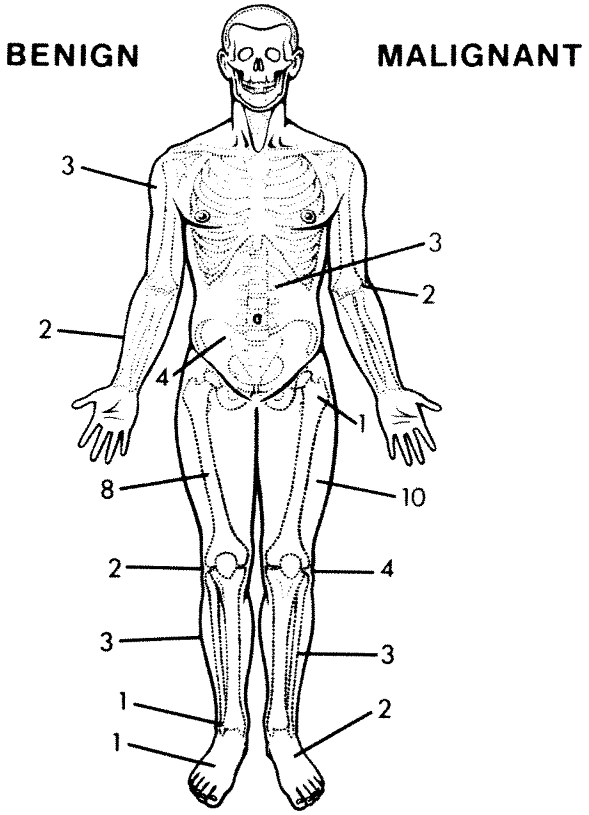


Figure 1. Distribution of primary soft-tissue tumours (24 benign, 25 malignant).

defined, one from poorly to well defined and one from well defined to partially defined. In the benign category, 16 tumours were well defined, three partially defined and two poorly defined on both T_1- and T_2-WI. Two changed from partially to well defined, and one from well to partially defined. In the benign category, 16 tumours were well defined, three partially defined and two poorly defined on both T_1- and T_2-WI. Two changed from partially to well defined, and one from well to partially defined.

Discussion

It is generally accepted that soft-tissue tumours are better demonstrated with MRI than with CT or ultrasound (Petasnick et al, 1986; Totty et al, 1986; Chang et al, 1987; Demas et al, 1988; Sundaram et al, 1988; Kransdorf et al, 1989a; Berquist et al, 1990). The major advantages of MRI are its ability to display contrast between tissues and its capacity for multiplanar imaging. Recent investigations attempting to use MRI to distinguish benign tumours from malignancies have been inconclusive (Pettersson et al, 1987; Sundaram et al, 1988; Kransdorf et al, 1989a). Our study suggests that tumour septation and changes in homogeneity may be useful in predicting malignancy, and that characteristic appearances of certain benign masses further aids differentiation.

Although the shape of the tumour is non-specific, the presence of low-signal septation strongly suggests malignancy. This feature has been mentioned in other reports of soft-tissue sarcomas but its relationship to malignancy has not been emphasized. A septated appearance was described by London et al (1989) in their series on liposarcomas. Kransdorf et al (1989a) in their paper on soft-tissue tumours showed similar septation in illustrations of myxoid liposarcoma and neurofibrosarcoma but did not discuss this as a feature of malignancy. Similarly, Demas et al (1988) illustrated a soft-tissue sarcoma with low-signal septation. In our series, this septated appearance was apparent in 20 out of 25 of the malignant tumours (80%), in contrast with only two out of 24 of the benign tumours (8%). While it is not surprising that 18 out of 20 septated malignant tumours were spindle cell types since they are of mesenchymal origin, it is noteworthy that none of the benign spindle cell tumours in our series showed this septated morphology.

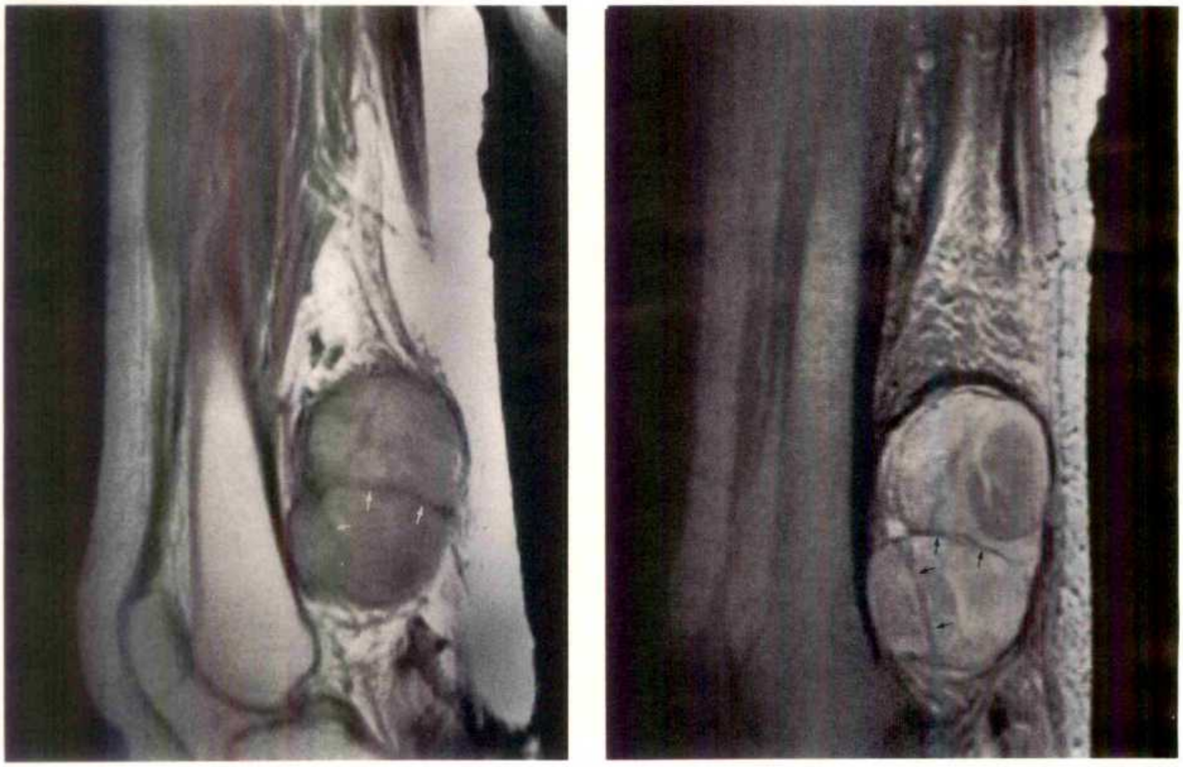
Malignant fibrous histiocytoma (MFH) was the most common tumour in our series. 10 of the 12 cases of MFH had a lobulated appearance both on T_1- and T_2-WI, consisting of irregular nodular masses separated by fine low-signal-intensity bands. This feature was also seen in our three synovial sarcomas. Septation in liposarcomas has previously been described by London et al (1989), who believed that septation represented a more differentiated fatty component in the tumour. Alternatively these low-signal septa may represent streaks of fibrous tissue or regions of relative acellularity. One can speculate that non-uniform stages in the growth of tumours may be separated by fibrous tissue and show a pattern of septation.

Although this appearance is highly suggestive of malignancy, it is not infallible. Two benign tumours, an abscess and an atypical lipoma, showed this appearance and were mistakenly diagnosed pre-operatively as malignant. In a recent report, an intramuscular myxoma was mistakenly but reasonably diagnosed pre-operatively as a liposarcoma because of similar septation (Kransdorf et al, 1989a).

In the absence of septation we found no significant patterns that differentiate benign nerve sheath tumours from their malignant counterparts. In all instances they were well demarcated from the neighbouring structures.

One benign Schwannoma and two malignant Schwannomas appeared homogeneous on T_1-WI and heterogeneous on T_2-WI. None of the benign Schwannomas showed evidence of septation. Thus, while the absence of septations does not exclude a malignancy, their presence is strongly against a benign process.

The second criterion we found useful was whether the tumour was homogeneous or heterogeneous and if there was any change in pattern that occurred from T_1-WI to T_2-WI. The pattern of 18 of the 25 malignancies (72%) changed between T_1-WI and T_2-WI, with 16 of the 18



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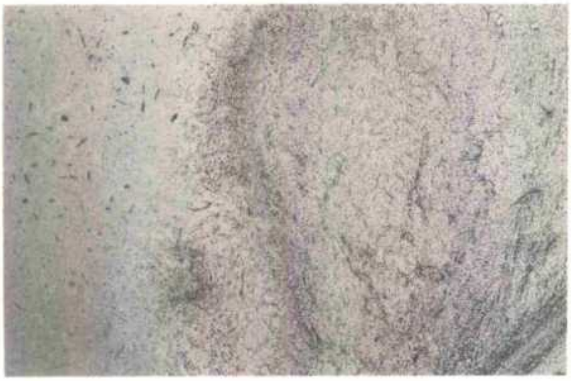

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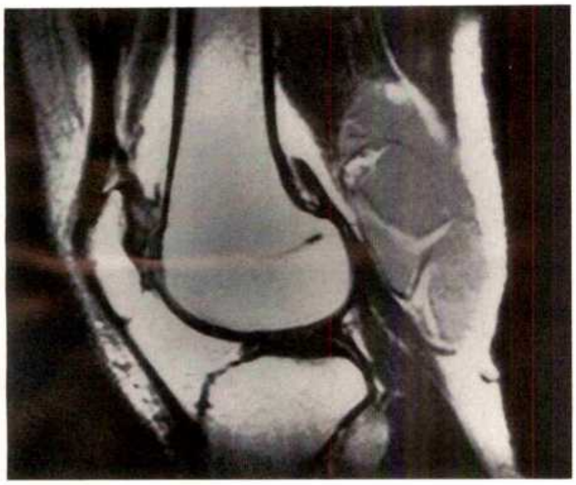
Figure 2. Malignant fibrous histiocytoma in a 72-year-old woman. (a) Sagittal image shows a slightly higher signal intensity mass behind the distal femur on T_1-WI (SE 600/30). (b) On T_2-WI (SE 1800/100) the mass shows high signal, is heterogeneous and well defined. Note the low-signal-intensity septa (arrows) causing lobulation on both T_1- and T_2-WI. (c) Malignant fibrous histiocytoma. Low power shows adjacent myxoid areas with cellular fibrous septa between them corresponding to an area of decreased signal intensity on T_2-WI (centre) (× 11).

homogeneous on T_1-WI and heterogeneous on T_2-WI. Only three of 24 benign tumours (12.5%) behaved similarly. Thus it appears that the change from a homogeneous pattern to a heterogeneous one is of prognostic significance. The majority of benign tumours (67%) maintained their original pattern of homogeneity on both T_1- and T_2-WI sequences. Moreover, of all the tumours in our series, nine were homogeneous on both sequences, of which eight (89%) were benign. If one examines only T_2-WI, our data agree with that of Petasnick et al (1986) who concluded that on T_2-WI, benign lesions tend to be more homogeneous than malignant tumours. Indeed, of our 49 tumours, 18 were homogeneous on T_2-WI, of which 13 (72%) were benign. However, we emphasize that it is the change of the tumour from the T_1-WI pattern to the T_2-WI pattern that is important and not the isolated appearance of one without the other. Therefore, in each case both sequences should be carefully evaluated.

The criteria of signal intensity and margin definition were generally not helpful. Almost all soft-tissue tumours are of high signal on T_2-WI, and lesions that demonstrated high signals in both sequences were almost equally divided between benign and malignant.



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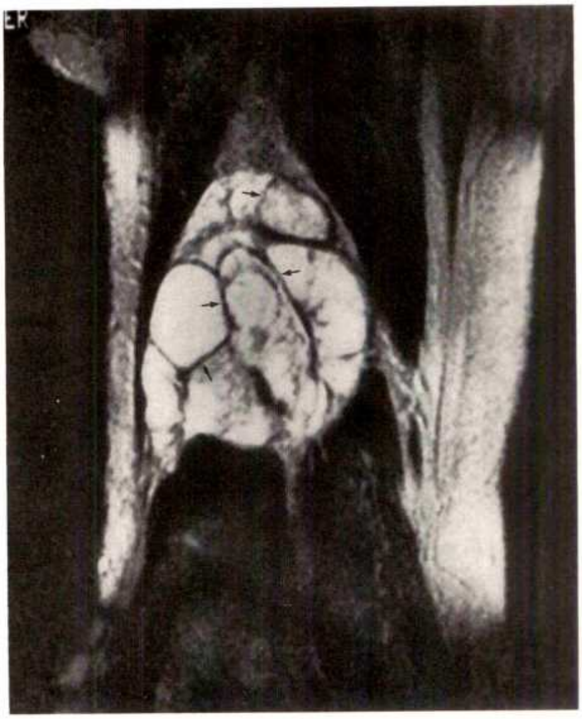

(b)

Figure 3. Liposarcoma of the popliteal region in an 18-year-old male. (a) Sagittal T_1-WI (600/30) shows septation. (b) Coronal T_2-WI (2100/80) appears heterogeneous with exterior low-signal-intensity septa that divide the mass into smaller lobules (arrows).

However, those tumours that were isointense on T_1-WI and of high signal on T_2-WI were predominantly malignant.

In addition, certain characteristic benign patterns have been described with which the findings in our cases concur; for example, PVNS is isointense on T_1-WI and T_2-WI (Kottal et al, 1987; Jelinek et al, 1989) and ganglia (Totty et al, 1986; Petasnick et al, 1986) and myxomas (Kransdorf et al, 1989) are low on T_1-WI and high on T_2-WI. In our series, desmoids gave a low signal on both T_1-WI and T_2-WI. These characteristic appearances are important because they aid in the recognition of these processes as benign. For example, despite the infiltrative, locally aggressive nature of desmoid tumours mentioned by Berquist et al (1990), the persistent low signal intensity on both T_1-WI and T_2-WI should strongly suggest the diagnosis. The underlying pathological explanation for these appearances is the presence of fluid in ganglia and myxomas, dense fibrotic tissue in desmoids, and intra and extracellular haemosiderin in PVNS. Similarly, decreased signal owing to haemosiderin deposition has been observed in cases of repeated transfusion for thalassaemia (Brasch et al, 1984). In one case of MFH in which myxomatous tissue was predominant, the tumour was isointense on T_1-WI and of homogeneously high signal on T_2-WI (Fig. 4). Sundaram et al (1987) found that tumours which are relatively acellular and contain a large amount of collagen show relatively low signal intensity on T_2-WI, and concluded that the cellularity of a tumour rather than the histological diagnosis influences the MRI signal on T_2-WI.

Petasnick et al (1986) and Berquist et al (1990) suggest that benign masses show well defined borders. Our data generally agree with this finding, although in our series it was not reliable enough to be useful in distinguishing benign from malignant lesions.

In summary, our findings suggest that tumours which change in homogeneity from T_1-WI to T_2-WI, and especially those that alter from a homogeneous pattern to a heterogeneous pattern, are more likely to be malignant. Lesions that do not change, and especially those that remain homogeneous, are most likely benign. In addition, tumours with septation are most likely malignant, and probably of spindle cell origin. Where these two criteria conflict (*i.e.* a lobulated tumour that does not change pattern), we believe that the presence of low-signal septation is a stronger predictor of malignancy than a change in pattern.

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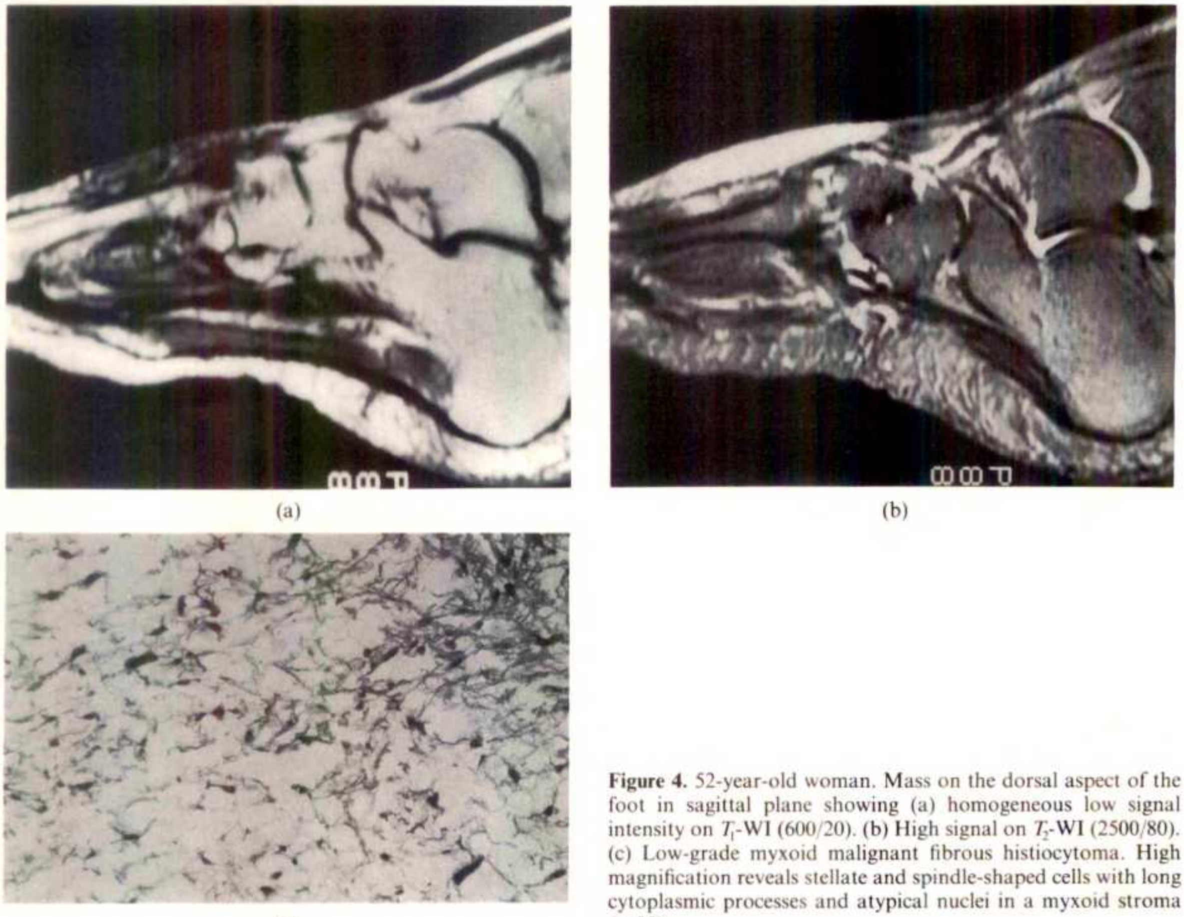

(a)

(b)

(c)

Figure 4. 52-year-old woman. Mass on the dorsal aspect of the foot in sagittal plane showing (a) homogeneous low signal intensity on T_1-WI (600/20). (b) High signal on T_2-WI (2500/80). (c) Low-grade myxoid malignant fibrous histiocytoma. High magnification reveals stellate and spindle-shaped cells with long cytoplasmic processes and atypical nuclei in a myxoid stroma (× 88).

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^{99}Tc^{m}-mercapto acetyl triglycine in paediatric renal tract disease

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Abstract. The use of ^{99}Tc^{m}-mercapto acetyl triglycine (^{99}Tc^{m}-MAG3), a new hippuran substitute, has been reported widely in adults but not in children. Our experience of its use in 100 infants and children for renography and indirect micturating cystography (IMC) is reported. The average age was 5.6 years. 65 patients completed IMC studies and nine patients had ^{99}Tc^{m}-dimercaptosuccinic acid (^{99}Tc^{m}-DMSA) scans performed on the same day. The majority of patients were referred for the investigation of urinary tract infection. 32 kidneys were found to be scarred on ^{99}Tc^{m}-MAG3 scans, 17 kidneys and ureters refluxed on IMC and 14 kidneys were obstructed. The results of ^{99}Tc^{m}-MAG3 scans were compared with those of other urinary tract investigations including ultrasound, micturating cystography (MCUG), intravenous urography (IVU) and ^{99}Tc^{m}-DMSA scintigraphy. No kidney which was scarred had a normal ^{99}Tc^{m}-MAG3 scan. All significant degrees of dilatation or obstruction on IVU or ultrasound were also detected by ^{99}Tc^{m}-MAG3. ^{99}Tc^{m}-MAG3 gave more information than any other single imaging modality and we believe it represents an ideal initial screening test in the investigation of urinary tract infection in older toilet-trained children.

^{99}Tc^{m}-mercapto acetyl triglycine (^{99}Tc^{m}-MAG3) is a recently developed radiopharmaceutical with similar properties to hippuran. Like ^{131}I- and ^{123}I-hippuran, ^{99}Tc^{m}-MAG3 is secreted by the renal tubules and, therefore, has a rate of excretion more than 3 times that of ^{99}Tc^{m}-DTPA, which is a glomerular filtrate, with 73% excreted by 30 min (Taylor et al, 1986). The use of ^{99}Tc^{m} as a label has practical advantages over ^{131}I, which is poorly suited to most modern gamma cameras, and ^{123}I, which is expensive and less readily available (Merrick, 1989). Use of this compound in adults has been well documented (Al-Nahhas et al, 1988; Schaap et al, 1988) but its use in children has not been widely reported. This paper describes our experience of its use in the investigation of renal tract disease in a district general hospital in 100 consecutive children for renography and indirect micturating cystography (IMC).

Patients and methods

100 infants and children who had ^{99}Tc^{m}-MAG3 scans performed between January 1988 and October 1989 were included in the study. The notes, radiological investigations and radionuclide scans of all patients were reviewed. There was no retrospective reporting of any investigation. Each kidney and ureter (renal unit) was considered separately when comparing results.

A freeze-dried commercially available MAG3 kit (Mallinckrodt Diagnostica) was labelled with 600 MBq (16 mCi) of ^{99}Tc^{m}. Vials were stored at 2–4°C and used within 4 h. ^{99}Tc^{m}-MAG3 scans were performed following oral hydration based on an adult dose of 100 MBq (2.7 mCi) 1.73 m^{-2} scaled according to body surface area. 10 patients required intravenous midazolam sedation and 25 received intravenous frusemide for the assessment of dilated upper tracts. Patients were studied supine on a 300 mm IGE gamma camera and data collected using a 64 × 64 matrix in 180 × 10 s frames via a Link Maps 5000 computer as well as gamma camera images using a 128 × 128 matrix in 2.5 min frames.

Micturating studies were performed at the end of the 30 min renography phase with the patient sitting on a modified commode. 2 s frames were acquired during micturition from which time/activity curves for both renal and, where there was sufficient ureteric activity, ureteric regions of interest were plotted. Urine flow rates and residual volumes were also calculated following the method described by Van Der Vis-Melson et al (1988).

To determine the reliability of relative function measurements using ^{99}Tc^{m}-MAG3, nine patients in whom ^{99}Tc^{m}-DMSA scans were clinically indicated had both investigations performed on the same day. In these patients the ^{99}Tc^{m}-DMSA injections were given at the end of the ^{99}Tc^{m}-MAG3 examinations and they were imaged 4 h later by which time there was no significant ^{99}Tc^{m}-MAG3 activity. Routine posterior and both oblique images were acquired using a 128 × 128 matrix.

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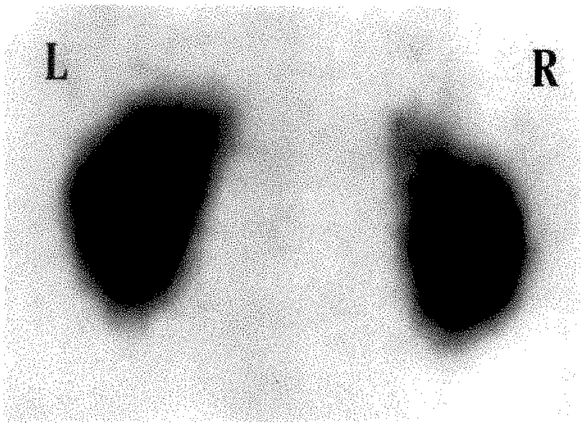

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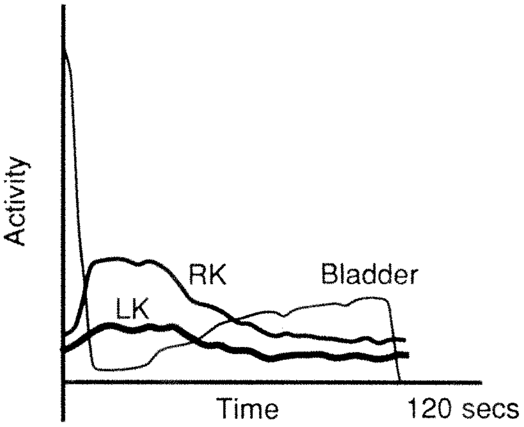

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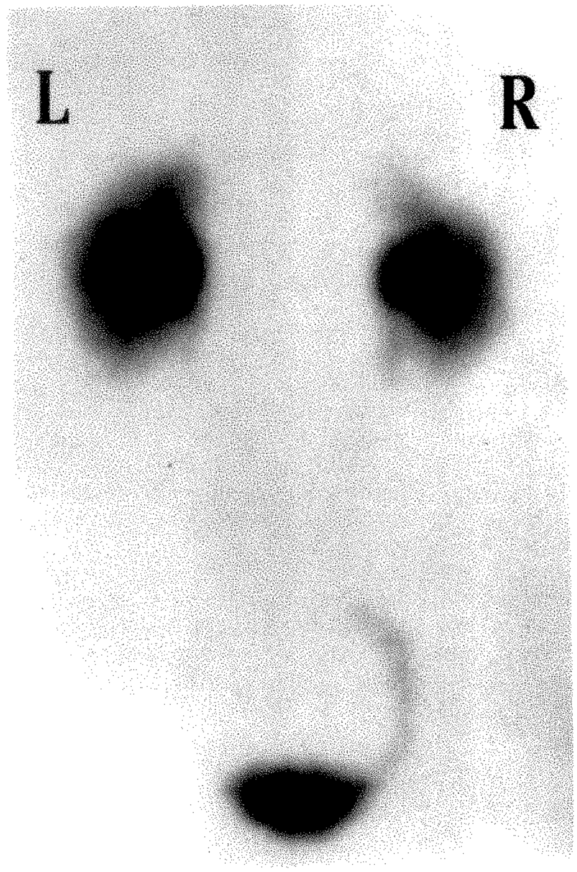

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Figure 1. (a) 2.5 and (b) 5 min ^{99}Tc^{m}-MAG3 images showing a focal scar at the right upper pole. (c) Time/activity curves showing bilateral reflux into the renal pelvis, more severe on the right, in a 6-year-old boy with recurrent urinary tract infections. Differential function 46% right, 54% left.

Results

The age range was 6 days to 17 years (mean 5.6 years), 18 patients were aged less than 1 year and 51 were under 5 years. 65 patients were deemed to have successfully completed IMC studies, although six of these were infants who micturated spontaneously during the study. The youngest patient to have a successful IMC, other than these six children, was 2 years 4 months. In 27 patients micturating studies were not attempted; in 16 because the patient was too young. Micturating studies failed in eight patients because they were unable to micturate; one of whom had been sedated.

The normal range of relative function for the right kidney was taken as 49.1 ± 5.2% and for the left it was taken as 50.9 ± 5.2%, and time to peak for the whole kidney 291 ± 121 s (Taylor et al, 1988). The quality of the 2.5 min parenchymal images obtained together with the underlying calyceal appearances allowed parenchymal scars to be detected. Kidneys were classified as showing focal scarring if there were discrete photon deficient areas on the 2.5 min images with or without underlying dilatation of the collecting system on subsequent images (Fig. 1). Global scarring was defined as a global reduction in relative function together with a uniform loss of cortical thickness, as shown by comparison of the 2.5 min parenchymal images with later images of the underlying collecting system.

Table I. Reasons for referral

	Number of patients
Urinary tract infection	57
Pre- or post-surgical assessment	21
Further assessment of antenatally diagnosed renal tract anomaly	13
Multiple congenital defects	4
Screening	3
Loin pain	2

Patients were grouped according to the reasons for referral (Table I). The three patients in the screening group were referred because they had siblings with reflux nephropathy. Other urinary tract investigations performed, although not necessarily concurrently, are shown in Table II.

Table III lists the main findings. These groups were not mutually exclusive, many of the scarred kidneys falling into the refluxing or obstructed groups as well. Nine of the scarred kidneys had focal scars, the rest showed global parenchymal loss. There were five globally scarred and two focally scarred kidneys in the under 1 year age group, and two globally scarred and one focally scarred kidney in the 1–2-year-old age group. IMC detected all grades of reflux including 5 units in three patients with Grade I reflux, although for purposes of comparison renal units were classified only as showing reflux or not. The group with reduced function did not include kidneys which were scarred. Eight kidneys were obstructed at the level of the pelvi-ureteric junction (PUJ).

Comparison with ^{99}Tc^{m}-DMSA

Figure 2 shows a graph comparing the differential function measurements, as determined by ^{99}Tc^{m}-DMSA, with ^{99}Tc^{m}-MAG3 scans of 12 patients who had both investigations done either on the same day or within 2 months of each other.

Table IV compares both investigations for the detection of scarring in all the patients who had ^{99}Tc^{m}-DMSA scans. 14 (50%) of these patients had studies performed within 3 months of each other and included nine of the 17 kidneys which were scarred on ^{99}Tc^{m}-DMSA or ^{99}Tc^{m}-MAG3. Despite an average time interval between scans of 9.5 months, there was good correlation with a sensitivity of 82% and specificity 95% (Fig. 3).

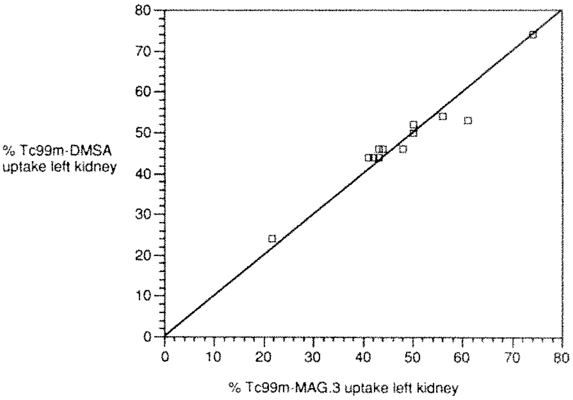

Figure 2. Graph showing percentage renal uptake of left kidneys as measured by ^{99}Tc^{m}-DMSA and ^{99}Tc^{m}-MAG3. Correlation coefficient 0.95 ($p < 0.0001$). The line of unity is shown.

Table II. Other urinary tract investigations

	Number of patients
Ultrasound	72
MCUG	44
IVU	42
^{99}Tc^{m}-DMSA	28

Table III. ^{99}Tc^{m}-MAG3 findings

	Number of kidneys/renal units
Scarred	32
Dilated	24
Reflux	17
Obstructed	14
Reduced function	13
Duplex	8
Dysplastic/absent	7
Horseshoe	1
Ureterocoele	1

Three kidneys which were not shown to be scarred on ^{99}Tc^{m}-MAG3 were shown to be focally scarred on ^{99}Tc^{m}-DMSA. In two of these, one of which had a normal IVU, the ^{99}Tc^{m}-MAG3 showed reduced differential functions of 43% and 42%. In the third patient the ^{99}Tc^{m}-DMSA scan showed a small focal scar seen only on the posterior oblique image. This was not seen on the ^{99}Tc^{m}-MAG3 scan performed 1 year later (Fig. 4), although IMC confirmed continuing reflux into the renal pelvis.

There were two kidneys in which scars were apparently not detected by ^{99}Tc^{m}-DMSA. Both of these were in obstructed systems. In one patient the ^{99}Tc^{m}-MAG3

Table IV. Comparison of ^{99}Tc^{m}-DMSA with ^{99}Tc^{m}-MAG3 for the detection of scarring (55 kidneys in 28 patients)

^{99}Tc^{m}-DMSA	^{99}Tc^{m}-MAG3	
	Scar	No scar
Scar	14	3
No scar	2	36

Table V. Comparison of IVU with ^{99}Tc^{m}-MAG3 for the detection of scarring (84 kidneys in 42 patients)

IVU	^{99}Tc^{m}-MAG3	
	Scar	No scar
Scar	13	0
No scar	9	62

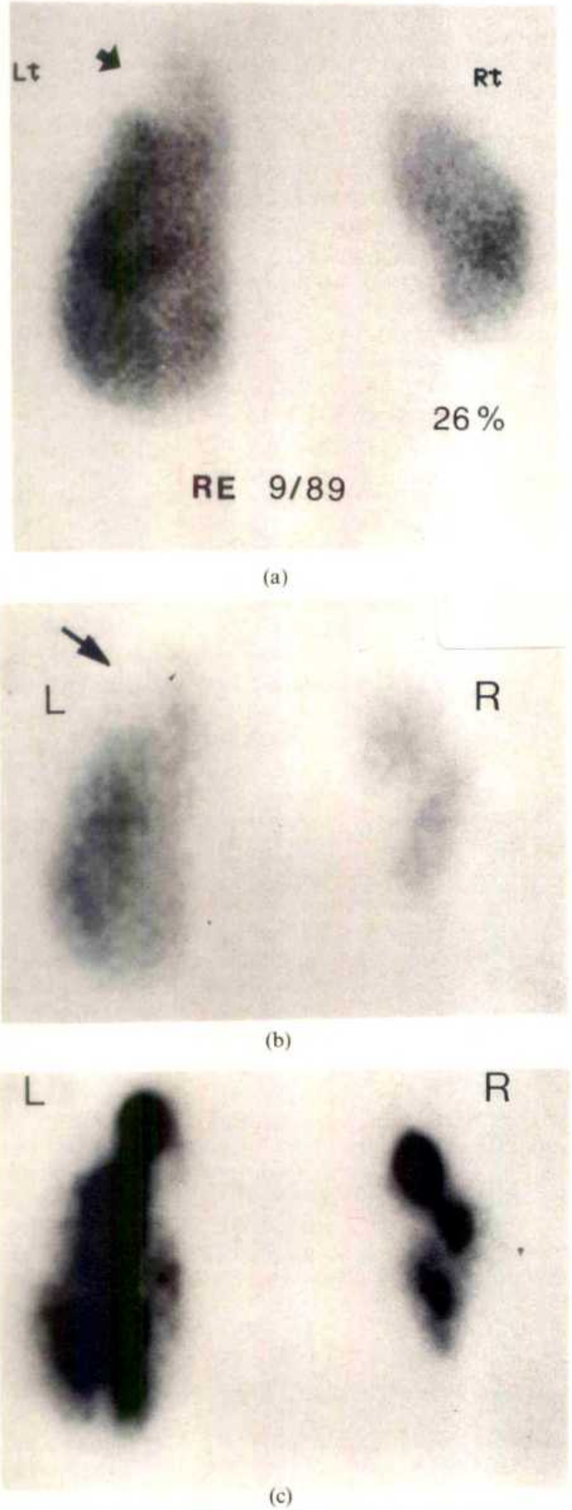

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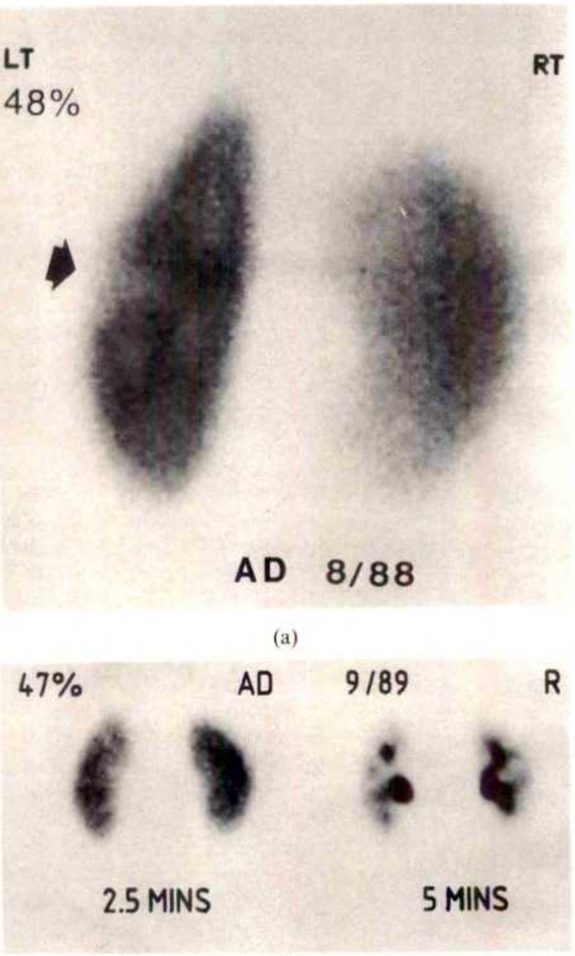
Figure 3. (a) ^{99}Tc^{m}-DMSA scan (posterior view). (b) and (c) The 2.5 and 5 min ^{99}Tc^{m}-MAG3 images of a 6-year-old boy with reflux nephropathy showing a globally scarred right kidney and a focal scar at the left upper pole (arrows).



(a)

(b)

Figure 4. Example of a focal scar (arrow) seen on the ^{99}Tc^{m}-DMSA left posterior oblique view (a) which was not apparent on the ^{99}Tc^{m}-MAG3 images (b).

was performed 14 months later in a kidney with PUJ obstruction and, in the second patient, 2 months later following surgery for the relief of an obstructive duplex system.

Comparison with IVU

Table V shows a similar table for the comparison of ^{99}Tc^{m}-MAG3 with IVU in the detection of scarring. Of the nine kidneys not showing scarring on IVU, six scans were performed from 1 to 4 years after the IVU in renal units with known Grade II–IV reflux. Of these, four had a differential function of less than 30%, in two of these a

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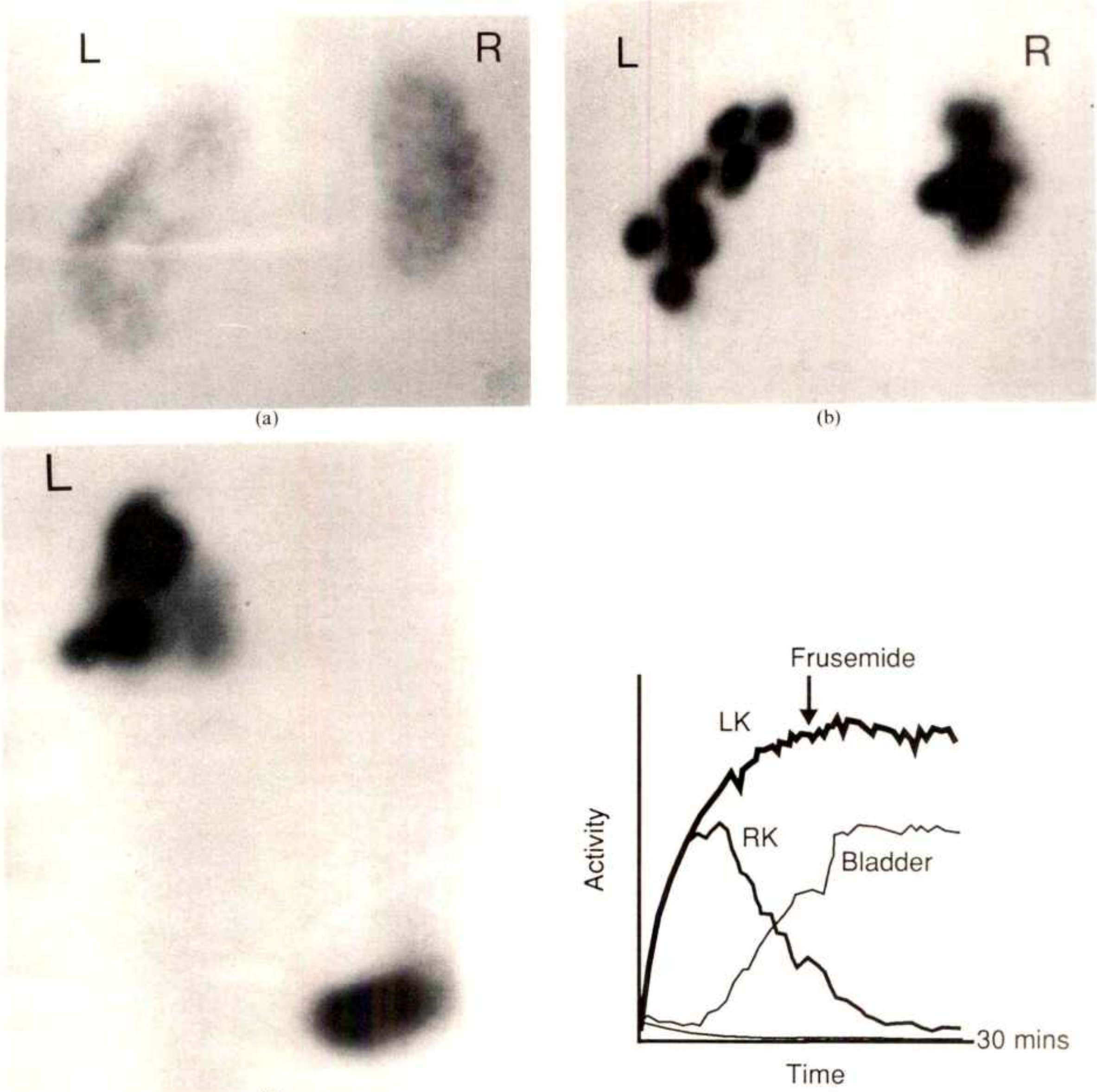
Differential function 26% right, 74% left on ^{99}Tc^{m}-MAG3. These scans were performed on the same day. IMC using ^{99}Tc^{m}-DTPA had previously shown bilateral reflux. On this occasion IMC confirmed continuing reflux into the left renal pelvis.



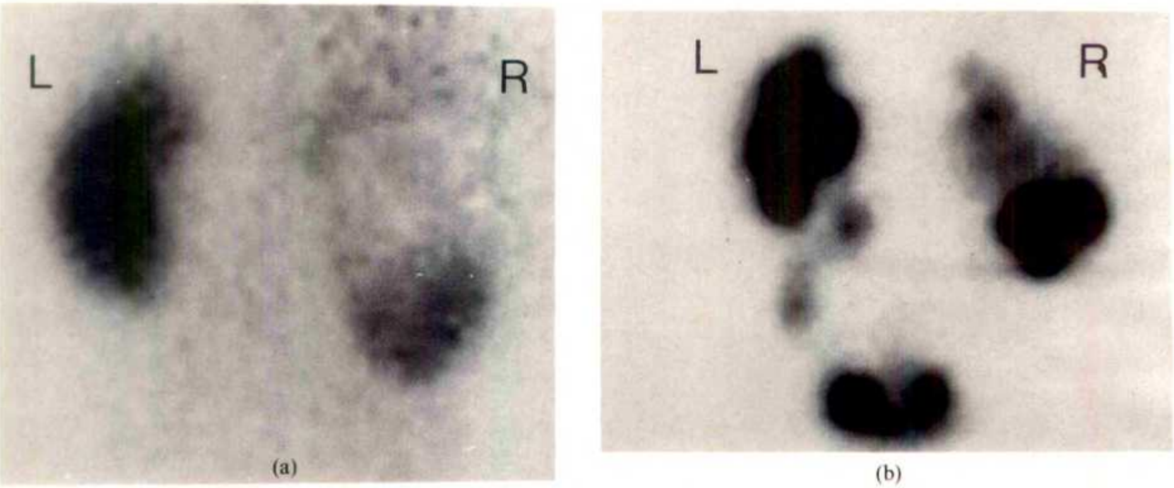
(a) (b) (c) (d)

Figure 5. (a), (b) and (c) 2.5, 7.5 and 25 min ^{99}Tc^{m}-MAG3 images, respectively, of a 1-year-old boy who required sedation showing a normal right kidney and a PUJ obstruction on the left. Equal function. (d) Time/activity curves from the same patient showing a normal renogram curve on the right but no significant drainage from the left renal pelvis in response to frusemide.

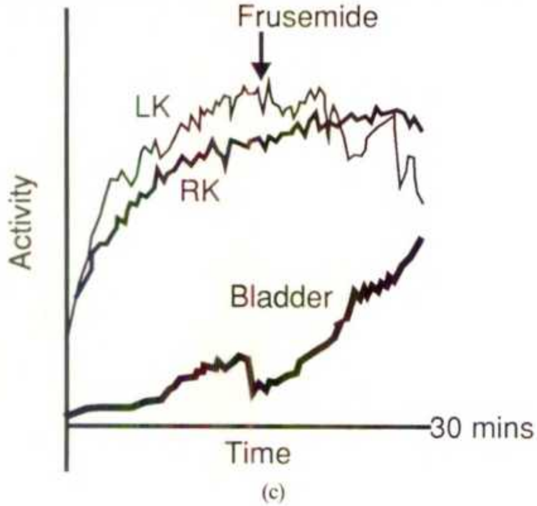
review of the IVU films revealed previously unreported scarring: one was in a patient with bilateral scarring and one was in a duplex system. In the remaining three kidneys, which were all obstructed systems, the nephrograms on the IVUs were too faint to allow comment regarding the presence of scarring. These are now all considered to represent false negative IVUs.

Obstruction

Obstruction was defined as a steadily rising renogram curve with a dilated collecting system in a well hydrated patient with normal renal function which failed to drain promptly following frusemide injection at 10–15 min. With the use of frusemide diuresis useful information was obtained concerning the nature, site and severity of obstructive uropathies (Figs 5 & 6). Of the 12 patients with obstruction on ^{99}Tc^{m}-MAG3 only five had IVUs and two ^{99}Tc^{m}-DTPA scans. The time interval between these investigations, frequently with intervening surgery, precluded useful comparisons. Nevertheless, all significant degrees of obstruction or dilatation demonstrated by IVU or ultrasound were also shown by ^{99}Tc^{m}-MAG3.



(a) (b)



(c)

Figure 6. (a) 2.5 and (b) 25 min images from the ^{99}Tc^{m}-MAG3 scan of a 2-month-old girl with a duplex right kidney and a large ureterocoele (seen as a filling defect in the bladder) which was causing bilateral obstruction. Satisfactory parenchymal images were obtained without the use of sedation showing a non-functioning upper moiety on the right. Different function 41% right, 59% left. (c) Time/activity curves demonstrating no response to frusemide.

Comparison with MCUG

Table VI shows the results of IMC and MCUG in the 21 patients who had both investigations. There was correlation in 71% of renal units for the detection of reflux despite an average time interval between investigations of more than 2 years.

Of the four renal units with reflux on IMC but not on MCUG, two were in a 4-month-old boy, interpreted as having bilateral reflux when he voided spontaneously at a time of high renal activity. The remaining two were in patients with bilateral reflux on IMC but only unilateral reflux on MCUG.

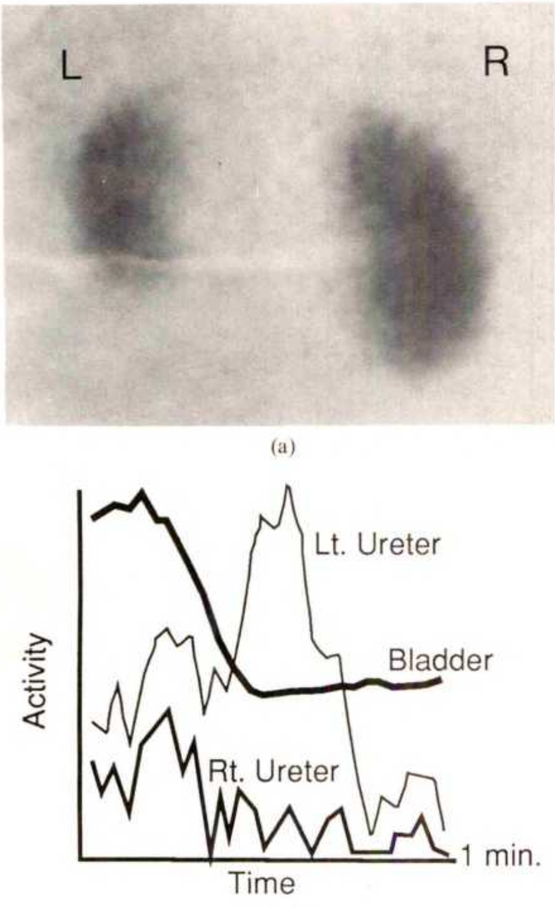
Of the eight renal units with reflux on MCUG but not on IMC, four were in patients with IMC studies performed 17 months to 4 years after MCUG. In one patient the IMC was performed following heminephroureterectomy. Another was again in a 2-month-old boy who voided spontaneously during the study. In one renal unit with Grade II reflux on MCUG, the ^{99}Tc^{m}-MAG3 study 1 year later showed probable yo-yo reflux in a scarred duplex system. In the remaining case the ^{99}Tc^{m}-MAG3 scan showed a globally scarred kidney with 28% differential function.

Discussion

Indirect radionuclide cystography was first described by Dodge (1963) using ^{131}I-hippuran. Many studies using ^{131}I or ^{123}I labelled hippuran or ^{99}Tc^{m}-DTPA have since shown it to be at least as sensitive as MCUG in the detection of reflux (Gordon, 1989). The advantages of IMC over MCUG include a lower radiation dose, con-

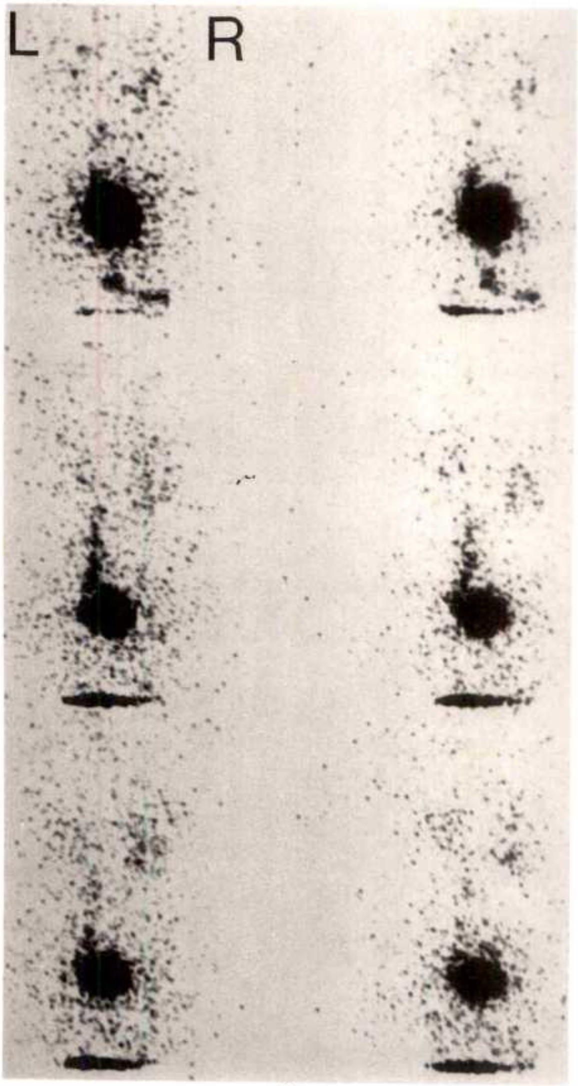
Table VI. Comparison of MCUG with IMC for the detection of all grades of reflux (42 renal units in 21 patients)

MCUG	IMC	
	Reflux	No reflux
Reflux	8	8
No reflux	4	22



(a)

(c)



(b)

Figure 7. (a) ^{99}Tc^{m}-MAG3 2.5 min parenchymal images from an 8-year-old girl with reflux nephropathy showing a globally scarred left kidney with differential function 28%. (b) IMC analogue images and (c) time/activity curves calculated from ureteric regions of interest confirming reflux into the left ureter (equivalent to Grade I). MCUG performed 4 years previously showed Grade III reflux on the right and Grade IV on the left. The IVU at the time was reported incorrectly as showing no scarring. ^{99}Tc^{m}-DMSA scan 1 year previously showed 33% differential function on the left.

tinuous screening, no catheterization and a more physiological examination. The main disadvantages are the lack of anatomical information and the prerequisite of a toilet-trained child. Despite this it has not yet gained wide acceptance amongst paediatricians or urologists as a technique for the detection of reflux.

^{99}Tc^{m}-MAG3 has a number of advantages over previous radiopharmaceuticals used for IMC. The three-fold increase in renal uptake of ^{99}Tc^{m}-MAG3 over ^{99}Tc^{m}-DTPA leads to an improved target to background ratio and a higher photon flux for a given administered activity. This gives superior image quality, allows use of shorter frame times for micturating studies (1 or 2 s instead of 5), enables relative function to be measured at as low as 2% of normal renal function as opposed to 12% for ^{99}Tc^{m}-DTPA (Jafri et al, 1988) and the entire study can be completed in half an hour instead of 2–4 h.

The improved sensitivity and increased target to background ratio allows low grades of reflux to be detected, including reflux into the ureter alone (Fig. 7), corresponding to Grade I reflux. It has been possible previously to detect Grade I reflux using direct radionuclide voiding cystography (Willi & Treves, 1985), although most studies using indirect radionuclide cystography have only recorded reflux into the renal pelvis, with few attempting to distinguish different degrees of reflux.

The degree of correlation in this study reflects both the intermittent nature and natural history of reflux (Cremin, 1979). A similar degree of correlation has been shown by other studies comparing MCUG with IMC using ^{99}Tc^{m}-DTPA or ^{123}I-hippuran (Merrick et al, 1977; Pollett et al, 1981; Carlson et al, 1986; Chapman et al, 1988). The inadvisability of attempting to interpret studies during which micturation occurred spontaneously is borne out by the two cases already mentioned. The continuing high renal activity in such cases will make the interpretation of reflux hazardous.

^{99}Tc^{m}-MAG3 is less effective for the detection of focal cortical scarring than ^{99}Tc^{m}-DMSA. This is because of the higher information density and multiple projections routinely imaged in the latter investigation. This disadvantage is offset partly by the benefits of a lower radiation dose, the additional information concerning drainage and reflux and a much shorter examination time. In addition, ^{99}Tc^{m}-DMSA may underestimate the degree of cortical scarring, particularly in instances where there is bilateral global cortical loss and thus equal function (McLorie et al, 1989; Whitear et al, 1990). This is less likely to occur with ^{99}Tc^{m}-MAG3 since visualization of the underlying calyces allows a better estimation of cortical thickness and the detection of dilated or obstructed collecting systems. The use of ultrasound to detect dilated collecting systems will help to avoid this particular drawback of ^{99}Tc^{m}-DMSA, although in our series ultrasound failed to detect two of the obstructed and eight of the dilated collecting systems. Ultrasound also failed to demonstrate cortical loss in four globally scarred kidneys.

To obtain adequate parenchymal images it is essential that the child remain still throughout the procedure. It is usually possible to hold very young infants still without the need for sedation although a small number of older infants and toddlers will require sedation, which should be given before the procedure. Using this technique we were able to obtain satisfactory studies in most of the younger children in this series.

The effective dose equivalent in an adult using an administered activity of 100 MBq 1.73 m^{-2} and based on a 3.5 h void is approximately 0.8 mSv (Taylor et al, 1988). The actual dose, particularly to the bladder wall and gonads, will be much less if the patient voids at 30 min as part of a micturating study. This compares with a dose of 1.89 mSv when using 300 MBq of ^{99}Tc^{m}-DTPA with a void time of 3.5 h. The effective dose equivalent when using 80 MBq of ^{99}Tc^{m}-DMSA is 1.28 mSv (ICRP, 1987), although the dose to bladder and gonads is negligible since it is not excreted. By contrast, the absorbed dose from an MCUG is 10–100 mSv. Some centres have taken advantage of the superior counting statistics of ^{99}Tc^{m}-MAG3 to decrease further the radiation dose by reducing the administered activity to 15 MBq 1.73 m^{-2}, although this does not give parenchymal images of diagnostic quality (Merrick, personal communication). We believe that the additional information obtained concerning the parenchymal appearances justifies the additional radiation dose from using the higher activity.

Our experience has shown ^{99}Tc^{m}-MAG3 renography and indirect radionuclide cystography to be an invaluable technique for the investigation of renal tract disease in children, providing more information than any other single imaging modality alone. In this respect we believe ^{99}Tc^{m}-MAG3 is ideal for the investigation and follow-up of obstructive lesions. It is ideal for the follow-up of differential function and also, given the reduction in radiation dose compared with MCUG of several orders of magnitude, for the follow-up of reflux in the older toilet-trained and cooperative child. Younger children will, at least initially, still require MCUG or direct isotope cystography for the investigation of reflux combined with ^{99}Tc^{m}-DMSA for the detection of scarring and ultrasound for assessment of upper tract dilatation. We consider ^{99}Tc^{m}-MAG3 renography and indirect cystography, combined with the use of ^{99}Tc^{m}-DMSA scans performed on the same day in those who have an abnormal ^{99}Tc^{m}-MAG3 study, to be a useful initial screening investigation in older children being investigated for urinary tract infection who represent our largest referral group.

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Chest radiography in the management of breast cancer

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Abstract. This study was undertaken to assess the utility of chest radiography (CXR) in the management of patients with breast cancer and to devise a suitable imaging policy for such patients. A retrospective analysis was performed of the case notes and the CXRs of a series of 141 patients presenting to this hospital in 1980 with a diagnosis of early breast cancer. Data retrieved covered the entire clinical course to date and included the number of CXRs performed for a clinical reason and the number performed as "routine". Correlation of the result of every CXR requested to subsequent therapeutic decision-making throughout the complete clinical course of each patient was undertaken and the proportion of CXRs initiating a management change, or performed for a clinical reason, out of the total requested was assessed. A total of 1161 CXRs were performed on the 141 patients studied. Of these, only 174 (15%) were undertaken for a direct clinical reason and 987 (85%) were undertaken as part of "routine" follow-up procedures and had no impact on patient management. Four "routine" CXRs (< 0.4%) demonstrated previously undiagnosed pulmonary metastases, in patients with no other history of metastatic disease. Thus, routine chest radiography is not a cost-effective method of monitoring asymptomatic patients with breast cancer for metastasis. It is recommended that outside staging procedures for clinical trials, the CXR is used only to address a clinical problem relating specifically to the thorax. It is anticipated that the cessation of all other chest radiography in patients being followed up for breast cancer at this institution will have significant budgetary implications.

There is little evidence that the finding of hitherto undiagnosed pulmonary metastases on a routine "follow-up" chest radiograph (CXR) improves the current outlook for the patient with early breast cancer (Horton, 1984; Dewar & Kerr, 1985; Ciatto et al, 1989; Rutgers et al, 1989). Indeed, despite the large battery of screening tests available to the clinician to monitor such patients (radiological, biochemical and otherwise), no survival benefit is conferred by the detection of any clinically occult metastatic disease and many workers now feel that tests on these patients should only be undertaken for new symptoms or clinical findings (Zwaveling et al, 1987; Mansi et al, 1988; Kindler & Steinhoff, 1989; Rutgers et al, 1989). The current emphasis on resource management, particularly in the field of oncology, demands rationalizing expenditure so that only the tests which contribute directly to patient care and outcome are employed, thereby allowing finite reserves to be directed most efficiently. With this in mind, the following study was undertaken to identify a role for chest radiography in the current management of breast cancer at all stages of the disease.

Methods

The case notes of a series of 141 patients presenting to the Royal Marsden Hospital, London during 1980 with early (non-metastatic) breast cancer were reviewed. Primary treatment with curative intent included mastectomy (75 patients) and local excision with axillary clearance (66 patients). 130 patients received post-operative irradiation depending on clinicopathological findings. The following information concerning all CXRs performed throughout the subsequent clinical course of each patient was retrieved:

(i) date and clinical reason given for CXR request,
(ii) radiologist's report of CXR, *i.e.* normal/abnormal (if abnormal: change/no change from previous examination),
(iii) total number of CXR examinations performed.

The outcome for each patient was documented, with follow-up to date (1990) whenever possible. The number of CXRs performed for a clinical reason in all patients was obtained and expressed as a fraction of the total. The pattern of CXR requests and the impact of the result on therapeutic decision-making was evaluated both for early and advanced disease.

Results

Of the 141 patients reviewed 50 (35%) subsequently developed recurrent or metastatic disease from which 43 patients have since died; 2 have died from other causes and 89 (63%) are alive and well at the last follow-up visit (mean follow-up period 8.7 years).

A total of 1161 CXRs were performed on 141 patients (Table Ia). Of these, 174 (15%) were requested either for new clinical symptoms or for a clinically-directed management problem (Table II) which relied on the CXR result. 987 (85%) CXRs were undertaken either as

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Table I (a). Overall results

Number of patients studied	141
Total number of CXRs performed	1161
Number of CXRs performed for a clinical reason (see Table II)	174 (15%)
Number of CXRs performed as "routine" follow-up, or for unidentifiable reason	987 (85%)

Table I (b). Number of CXRs undertaken according to patient outcome

Outcome	Number of patients (total = 141)	Number of CXRs	Number performed for a clinical reason	(%)
No recurrence/metastasis: (mean FU = 8.7 years)	91	634	14	2.2%
Local recurrence only	7	72	9	12%
Distant metastasis	43	455	151	33%

Table I (c). Number of CXRs undertaken according to site of first metastasis

Site of first metastasis	Number of patients (total = 43)	Number of CXRs	Number performed for a clinical reason	(%)
Lung/pleura	15	189	81	43%
Bone	18	164	45	27%
Liver	10	102	25	24%

part of a "routine" yearly follow-up procedure, or for unknown reasons not identifiable from the case notes and not resulting in a management change.

In four patients asymptomatic pulmonary metastases were identified on "routine" follow-up CXRs. This represents an asymptomatic yield in less than 3% of the total number of patients examined and less than 0.4% of the total number of "routine" CXRs performed. All four of these patients subsequently developed symptomatic metastatic disease (either pulmonary or bony) within 6 months (range 3–6 months) of the abnormal "routine" CXR and all have since died of their disease.

The group of 91 patients with no evidence of disease at last attendance had a total of 634 CXRs performed during follow-up (Table Ib), of which 14 (2%) were performed for clinical reasons as described in Table II.

Seven patients developed local recurrent disease (median time to recurrence: 21 months) and were treated successfully with surgery with or without radiotherapy; they are all well to date. A total of 72 CXRs were undertaken in this group, nine (12%) of these were performed for a clinical reason (usually pre-operative) and the remaining 63 (87%) were "routine" follow-up films.

43 patients developed distant metastatic disease and have since died. The median time from initial diagnosis to metastasis was 24 months, with median time to death being 38 months. The commonest site for initial metastasis was bone (18 patients), followed by lung and/or pleura (15 patients) and then liver (10 patients). A total of 455 CXRs were performed on these patients of these 151 (33%) were undertaken for clinical reasons (Table Ic) and 304 (66%) were performed either for reasons undocumented or for "routine" follow-up. Of the patients in whom the lung was the site of first metastasis, CXRs were performed with the greatest frequency and also with the greatest frequency of clinical indication.

Table II. Clinical reasons for CXR requests

(i) Thoracic symptoms: dyspnoea, pleuritic or rib pain, cough, chest infection, cardiac failure.
(ii) Monitoring response to chemotherapy or other treatment.
(iii) Monitoring interventional procedures: placement of chest drains, central lines, Hickman lines, management of pneumothorax.
(iv) Pre-operative.
(v) Investigation of other disorders, *e.g.* iron-deficiency anaemia.

Discussion

Overall, only 15% of all the CXRs performed on patients reviewed in this study contributed directly to their subsequent clinical management. Of the 91 patients followed up with no evidence of either local recurrence or distant metastasis, only 2% of CXR requests were undertaken for a clinical reason and only 33% of CXRs performed on patients who developed metastatic disease were shown to be of clinical value.

At this institution, the X-ray department performs approximately 2500 CXRs annually on patients with breast cancer at all stages of the disease. The yearly total of CXRs performed for all diseases in this department is around 9000, so imaging patients with breast cancer represents nearly one third of the overall CXR workload. The CXR is the single most frequent investigation requested at the Royal Marsden Hospital X-ray department, constituting over 60% of all plain film examinations undertaken.

Although early detection of local or regional recurrent breast cancer is undoubtedly worthwhile, there is much data to suggest that screening for asymptomatic metastatic disease in the follow-up of breast cancer is neither cost-effective nor beneficial to survival (Logager et al, 1990). Most studies, including this one, show a positive yield of less than 4%, both for routine chest radiography and for other tests, and the lead time conferred by the finding of such disease has not been clinically advantageous (Dewar & Kerr, 1985; Hughes & Courtney, 1985; Ciatto et al, 1989; Vestegaard et al, 1989). Many groups now advocate careful history taking and clinical examination for both the evaluation of local disease and distant relapse, with emphasis on flexible out-patient attendance depending on patient symptomatology, at which time only relevant tests are performed. However, the practice of standardized 6 monthly or yearly out-patient attendance involving a variety of investigations appears hard to change, perhaps because asymptomatic follow-up patients are often reviewed by relatively junior medical staff who may simply repeat the management policy of their predecessor.

The pattern of CXR requests in patients with known metastatic disease is also haphazard. This study has found that even in cases with known thoracic disease, only 43% of CXRs contributed usefully to therapeutic decision-making and of all patients who died of metastatic breast cancer, clinical reasons for CXR requests could only be found in one third of cases. In many instances, CXR requests on such patients were combined with requests for other radiographs, such as spinal and pelvic examinations during management of bony disease, for which the CXR result was irrelevant.

Clinical reasons for requesting CXRs in this study (Table II) include the pre-operative chest film, which was standard practice in this hospital in 1980 when this group of patients first presented. This practice has been rationalized over recent years in line with other units and the current policy at this institution is to perform such examinations on patients over the age of 50, or with a specific cardiac or pulmonary disorder justifying further investigation. The cost-effectiveness of performing routine pre-operative CXRs on all patients has been shown conclusively to be poor (Roberts et al, 1985). Its use as a staging procedure in the asymptomatic patient with early breast cancer is more controversial, but the positive yield in this circumstance is again extremely low (Feig, 1987).

By carefully reviewing all imaging policies, not only in breast cancer, so that only the examinations that contribute directly to patient management are performed, significant savings may be made within a financially constrained health service. Following this study, it is recommended that routine CXRs are not performed on patients being followed up after treatment for primary breast cancer at this institution. Chest radiography should be used to address specific clinical problems relating to the thorax, both in patients with early and advanced disease. It is estimated that reducing the number of unnecessary CXRs performed in this department on such patients will cut the overall CXR workload by over 2000 examinations annually, resulting in inevitable savings of both valuable budgetary resources and unnecessary irradiation to both patients and staff (NRPB, 1990).

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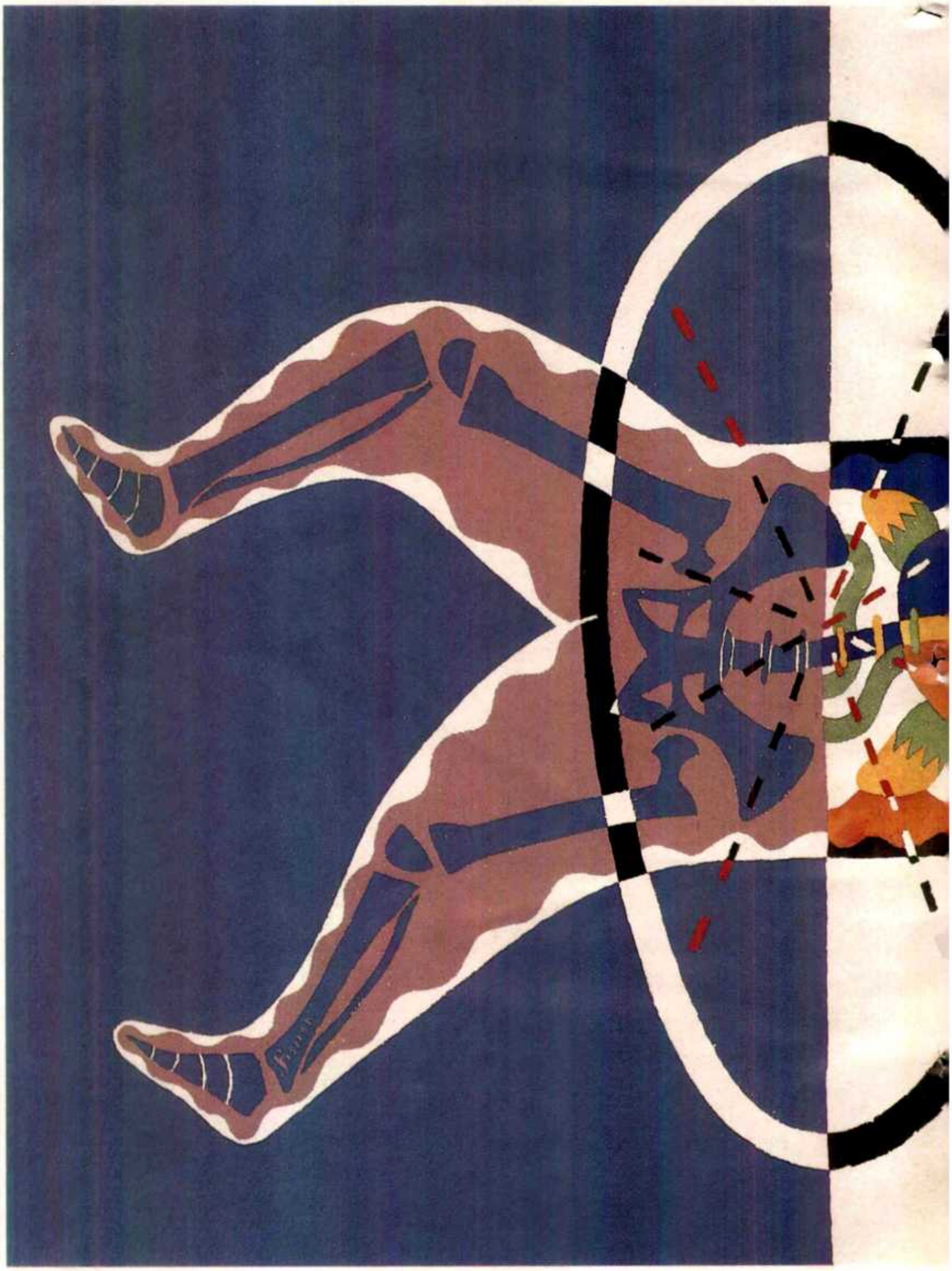

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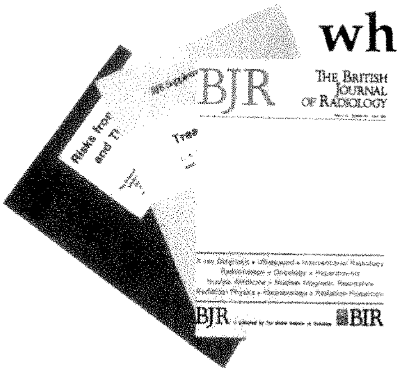

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Choledochal cyst and congenital anomalies of the pancreatico-biliary junction: the clinical findings, radiology and outcome in nine cases

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Abstract. Nine patients with choledochal cyst have been reviewed. There was a 6:3 preponderance of females. Four patients presented in adulthood. Cholangiocarcinoma developed in three patients with an interval ranging from 2 to 35 years following surgery. The predominant complaint was of abdominal pain and symptoms had been present from weeks up to 28 years. Imaging by sonography may be all that is required in the paediatric age group, but in adults further confirmation of the choledochal cyst and the associated anomalous junction of the pancreatico-biliary duct (AJPB) by direct cholangiography is recommended.

Choledochal cyst is a relatively rare disorder, usually diagnosed in infancy or childhood, although adult presentation is increasingly recognized (Flannigan, 1975). There is a close relationship between the choledochal cysts and the anomalous junction of the pancreatico-biliary duct (AJPB) (Todani et al, 1984), which provides a useful diagnostic sign, particularly in adults in whom duct dilatation is more commonly a result of other causes.

The main pancreatic duct and common bile duct normally unite within the sphincter of Oddi to form a common channel, termed the pancreatico-biliary duct, which opens into the second part of the duodenum. Both the junction and the pancreatico-biliary duct are governed by the sphincter. In the anomalous situation of the common duct being abnormally long, the junction lies beyond the influence of the sphincter. Two types of AJPB are recognized depending on whether the pancreatic duct appears to join the common bile duct or vice versa (Fig. 1).

Biliary carcinoma is known to be related to choledochal cyst (Bloustein, 1977) and more recently, the presence of the pancreatico-biliary (PB) type of AJPB has been shown to increase the risk of gallbladder carcinoma, even in the absence of choledochal cyst (Yamauchi et al, 1987). These relationships have been reviewed and are illustrated using our findings.

Patients and methods

Retrospective data from 1956 to 1988 were analysed in nine patients with proven choledochal cyst. The mode

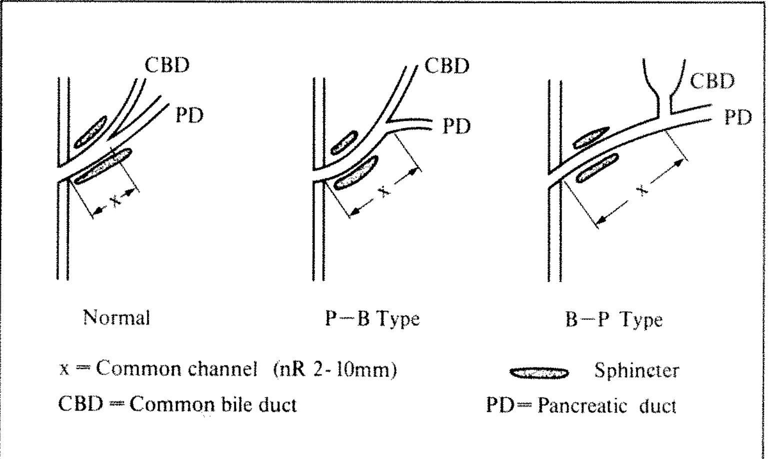

Figure 1. Normal and anomalous pancreatico-biliary union. If the pancreatic duct appears to join the common bile duct, this is designated BP Type. If the common bile duct appears to join the pancreatic duct, then this is designated PB Type.

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Table I. Summary of cases

Case	Sex	Age at presentation	Mode of initial presentation	Age at diagnosis of choledochal cyst	Methods of diagnosis of choledochal cyst	Treatment	Comment
1	M	51 years	Abdominal pain, choluria	51 years	Laparotomy, drainage tube—cholangiogram	Choledochocystectomy, hepaticojejunostomy, cholecystectomy	Died age 53 years of cholangiocarcinoma
2	F	9 months	No information	9 months	Laparotomy	Cholecystoduodenostomy	Died age 36 years of cholangiocarcinoma
3	F	30 years	Abdominal pain	30 years	Laparotomy	Cholecystoduodenostomy	Died age 34 years of cholangiocarcinoma
4	M	32 years	Abdominal pain	32 years	Ultrasound, drainage tube—cholangiogram	Choledochocystectomy, hepaticojejunostomy, cholecystectomy	Remains well 1 year post-operatively
5	F	37 years	Abdominal pain	37 years	Ultrasound, ERCP	Choledochocystectomy, hepaticojejunostomy, cholecystectomy	Remains well 5 years post-operatively
6	F	4 years	Jaundice, abdominal pain, fevers	10 years	Laparotomy, preoperative cholangiogram	Choledochocysto-duodenostomy, refashioned age 30 to hepaticojejunostomy	Hepatic fibrosis, recurrent cholangitis, alive 10 years post-operatively
7	F	2 years	Abdominal pain	30 years	Ultrasound, HIDA	Choledochocystectomy, hepaticojejunostomy, cholecystectomy	Remains well 2 years post-operatively
8	F	10 years	Abdominal pain	15 years	Ultrasound, ERCP	Choledochocystectomy, hepaticojejunostomy	Remains well 2 years post-operatively
9	M	4 years	Abdominal pain, vomiting	4 years	Ultrasound, ERCP	Choledochocystectomy, hepaticojejunostomy, cholecystectomy	Remains well 2 years post-operatively

of presentation, method of diagnosis, treatment and follow-up are summarized in Table I.

Results

The commonest presenting symptom was abdominal pain, a feature in eight cases. The available amylase estimations were normal in four instances (Cases 1, 3, 7 & 8). None of the cases had the classical triad of jaundice, pain and abdominal mass. Five patients (Cases 2, 6, 7, 8 & 9) were under 10 years of age at initial consultation, the remaining four were adults. There was a significant delay between the onset of symptoms and the diagnosis in three patients, ranging from 5 to 28 years (Cases 6, 7 & 8). Case 6, aged 4 years, had jaundice and hepatosplenomegaly and was diagnosed as having hepatic fibrosis. As this pre-dated sonography, the choledochal cyst was found 6 years later at laparotomy for persistent abdominal pain and cholangitis. There is a known association between choledochal cyst and hepatic fibrosis (Crittenden & McKinley, 1985). Cases 7 and 8 had had recurrent abdominal pain for many years, one was diagnosed by sonography aged 30 years and the other aged 15 years. Investigation by abdominal sonography in five cases was suggestive of choledochal cyst, although in one (Case 4), the appearance was initially thought to be an enlarged, folded gallbladder.

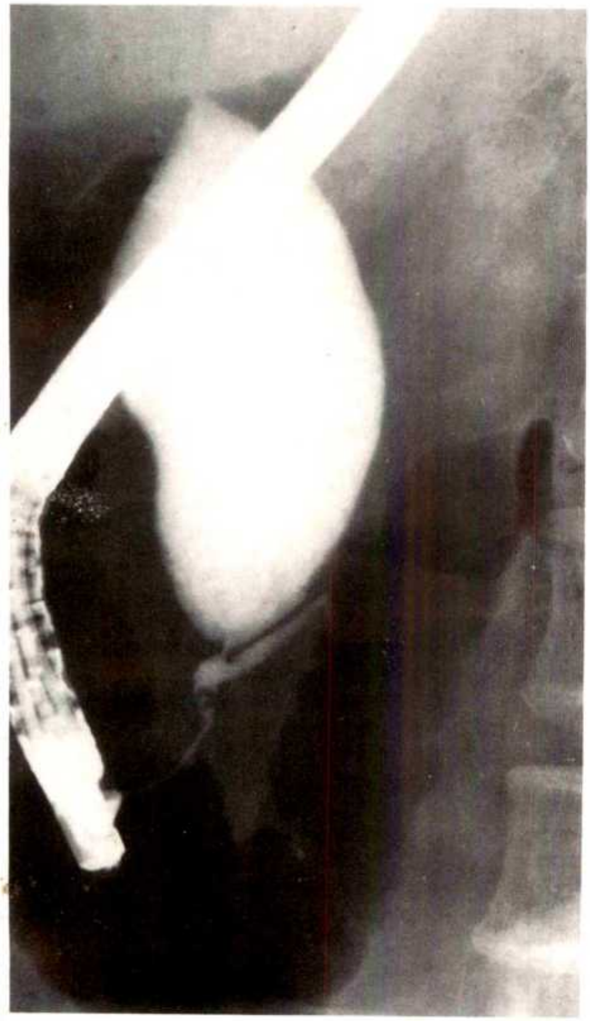

Figure 2. Choledochal cyst demonstrated pre-operatively by ERCP.

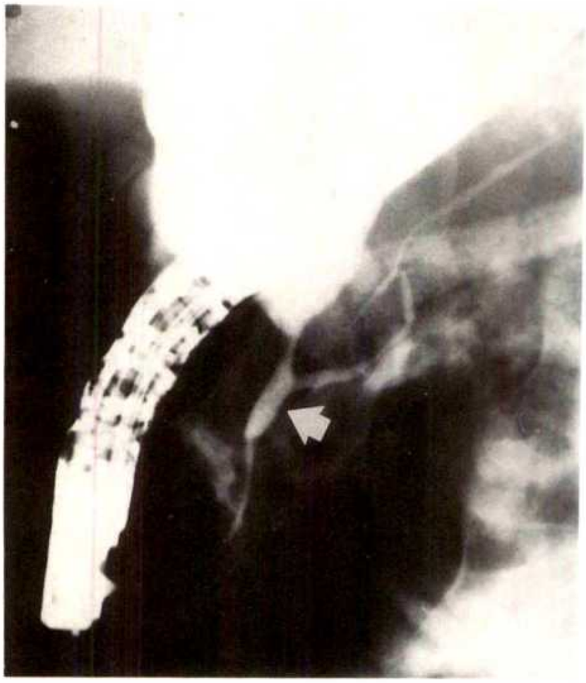

Figure 3. Anomalous pancreatico-biliary duct of the BP type at ERCP (arrow).

Direct cholangiograms were available in six cases (1, 4, 5, 6, 8 & 9). Three of these were diagnostic endoscopic retrograde choledocho-pancreatography ERCPs (Cases 5, 8 & 9) (Fig. 2). The remaining three underwent laparotomies and choledochal cysts were demonstrated on pre-operative cholangiography in Case 6 and post-operative cholangiography in Cases 1 and 4. AJPB was recognized in each of the six patients who had cholangiograms, three BP type and three PB type (Fig. 3). Intrahepatic bile duct dilatation of varying severity was observed in all cases. The size of the choledochal cysts varied between 3.5 cm and 5.0 cm in the maximum diameter.

Cholangiocarcinoma developed in three patients at intervals after the diagnosis of the choledochal cysts and original surgical treatment (Cases 1, 2 & 3). Case 1 underwent choledochocystectomy and hepaticojejunostomy 2 years previously and Cases 2 and 3 had had choledochoduodenostomy 34 and 4 years earlier. Percutaneous transhepatic cholangiography demonstrated extrahepatic biliary obstruction in each case (Fig. 4). At laparotomy, a large anastomotic tumour was found in Case 1 and extensive tumour related to

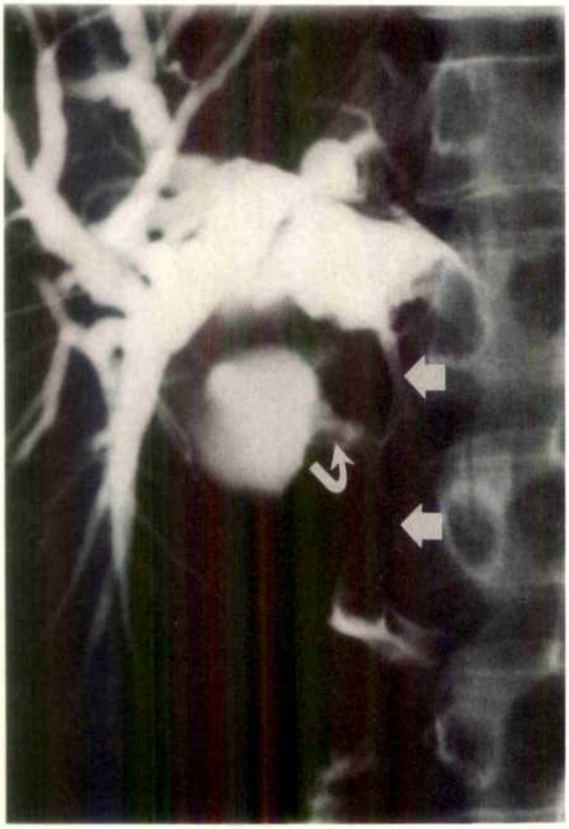

Figure 4. Case 2. Percutaneous cholangiogram. A large cholangiocarcinoma involving the choledochal cyst (broad arrows) and cystic duct (curved arrow).

the choledochal cysts were found in Cases 2 and 3. Histological proof of adenocarcinoma was obtained in each case and palliative bypass surgery performed. All three patients died of their disease within months of surgery.

Discussion

Choledochal cyst is a malformation of the biliary tree first described by Todd in 1817 (McConnel, 1919). The essential feature is cystic dilatation, most commonly of the extrahepatic biliary duct alone, but occasionally in association with the intrahepatic ducts. The widely accepted classification is that devised by Todani et al (1977), which is based on cyst morphology and location (Fig. 5). The classification encompasses a spectrum of cystic biliary changes which may have different aetiological origins. All the examples in our review are of Type 1, which comprises 80% of all choledochal cysts.

Two main aetiological theories have been put forward. In 1936, Yotuyanagi postulated an unequal proliferation of epithelial cells in the primitive bile ducts of the embryo. More recently, Babbit (1969) proposed that the dilation is acquired as the result of the anomalous junction of the pancreatico-biliary duct. Many authors have since reported an association between anomalous union and cystic bile duct changes. The incidence of AJPB coexisting with choledochal cyst ranges from 33% (Komi et al, 1977) to 100% (Jona et al, 1979). Babbit (1969) postulated that the anatomy of anomalous union allows the reflux of pancreatic juice at higher pressure into the bile duct, producing recurrent inflammation and eventual dilatation. There is evidence to support this theory in that high levels of pancreatic amylase have been detected in choledochal cysts (Kinoshita et al, 1984) and in experimental animals, cylindrical dilatation of the common bile duct has been induced by prolonged exposure to pancreatic juice (Oguchi et al, 1988). Choledochal cysts are reported more frequently to occur in association with the BP type junction (Yamauchi et al, 1987), but in one recent series (Kimura et al, 1985) this specific association did not emerge and there was no predominance in our limited series. No specific association between AJPB type and age of presentation was found.

The incidence of biliary malignancy in patients with choledochal cyst is higher than in the general popula-

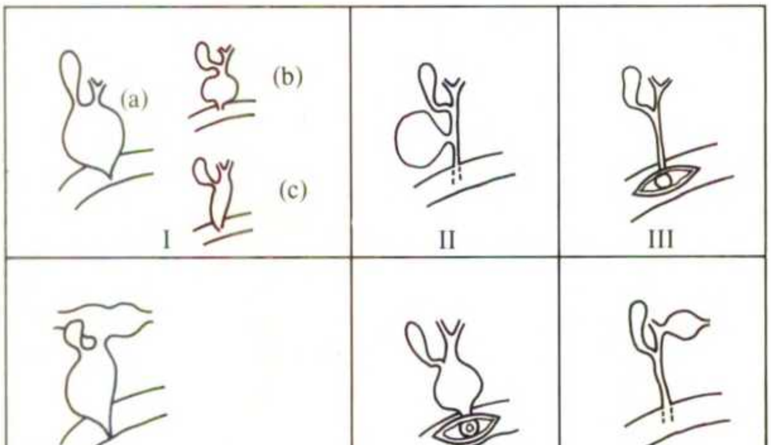

Figure 5. Classification of choledochal cysts according to Todani et al (1977) based on cyst morphology, position and multiplicity.

tion. One large review of 1433 patients revealed cyst carcinoma in 3.2% and gallbladder cancer in 1%, at an average age of 32 years (Yamaguchi, 1980). The association between gallbladder carcinoma and AJPB without choledochal cysts seems to be even stronger (Kimura et al, 1985). Moreover, those patients with an anomalous junction tend to develop malignancy about 10 years earlier than those without AJPB (Yamauchi et al, 1987). The vast majority of the junctions occurring with gallbladder cancer were found to be of the PB type.

Malignant change in the presence of AJPB may also be related to the reflux of pancreatic juices into the biliary tree, giving rise to chronic irritation and metaplasia (Kimura et al, 1985) and an ideal environment for such changes would be the stagnation found in a choledochal cyst or gallbladder. Our experience is in agreement with this concept, in that three of the patients developed cholangiocarcinoma at a relatively young age. In two patients, following bypass surgery alone, an extensive malignancy was discovered in relation to the cyst. The third patient had an anastomotic tumour recurrence as described by Thistlethwaite and Horwitz (1967), but this type of malignancy may also arise following biliary enteric diversions for other disorders (Herba et al, 1986).

The diagnosis of choledochal cyst is not always straightforward. The classical triad of pain, jaundice and abdominal mass occurs in a third of cases (Flannigan, 1975) and was not seen in our series, in which abdominal pain was the commonest finding. In the infant and young child, ultrasound alone will confirm the diagnosis. In adults, in whom the level of suspicion may be low, a cystic lesion in the porta hepatis or a grossly dilated bile duct should raise the possibility of a choledochal cyst. Approximately 20–60% of patients present in adulthood (Flannigan, 1975; Robertson & Raine, 1988). This may be partly caused by the late onset of symptoms and partly by the limited imaging methods in the past. Perhaps an acquired aetiology as put forward by Babbit (1969) would explain this delayed presentation. Confirmation of sonographic findings by further imaging is desirable in the older child and the adult. Isotopes are useful (Han et al, 1981) and like cholangiography will distinguish bile duct dilatation from other cystic lesions such as pancreatic cysts, double gallbladder and portal venous varix. Direct cholangiography is preferable as it will demonstrate the exact nature of any bile duct dilatation and provides the detailed biliary anatomy desired by many surgeons. ERCP, if available, will reliably demonstrate the associated AJPB, an important feature of the diagnosis. Percutaneous methods are adequate, but we contend that ERCP is less invasive and has the advantage of consistently demonstrating the pancreatic duct in which abnormalities may coexist (Rattner et al, 1983).

The accepted treatment of choledochal cyst involves excision and cholecystectomy because of the high incidence of malignant change. Some authors also advocate cholecystectomy and biliary reconstruction in cases of isolated AJPB, often found incidentally, because of the increased risk of gallbladder cancer (Nagata et al, 1985; Yamauchi et al, 1987).

We conclude that choledochal cyst is a diagnosis to be aware of in children and adults with upper abdominal pain and that sonography is the most useful preliminary examination. Direct cholangiography is desirable for confirmation in adults and treatment must involve cyst excision and cholecystectomy because of the risk of malignant change.

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Magnetization transfer contrast (MTC) imaging of skeletal muscle at 0.26 Tesla — changes in signal intensity following exercise

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Keywords: MRI, Magnetization transfer contrast, Muscle, Exercise

Abstract. Magnetization transfer contrast (MTC) imaging of skeletal muscle before and after exercise has been studied in normal volunteers at 0.26 Tesla. A saturation pulse was applied over a range of offset frequencies immediately before a gradient recall echo sequence. Substantial signal loss was observed in all muscles. After exercise, selective saturation resulted in a significant increase of contrast between active and less active muscle, a phenomenon attributable to an increase in extracellular water content. MTC imaging provides a more sensitive method to detect changes in water distribution in human skeletal muscle.

Relaxation coupling or cross relaxation is a phenomenon of energy transfer between two spin systems (Poole & Farach, 1971). Cross relaxation between the highly mobile "free" water protons ^1H_f and motion restricted "bound" water protons ^1H_r, associated with immobilized macromolecular constituents, plays a significant role in relaxation phenomena. A saturation transfer method, first described by Forsen and Hoffman (1963), has been adapted by Wolff and Balaban (1989) to image, *in vivo*, the cross relaxation process between "free" water and "bound" water. In this technique a relatively strong off-resonance radio frequency (RF) pulse is applied to saturate the proton spins in the restricted water. The subsequent chemical exchange and/or cross relaxation between spins of restricted water and "free" water result in a saturation transfer with substantial decrease in magnetization of the "free" water and consequent loss of signal. This new contrast governed by the magnetization transfer process was observed in magnetic resonance (MR) images of rabbit leg and kidney by Wolff and Balaban (1989), who coined the term "magnetization transfer contrast" (MTC). More recently, Baudouin et al (1990) and Tanttu et al (1990) have applied the technique to observe MTC in human subjects in clinical MR imaging systems.

We have studied the application of MTC in normal volunteers at 0.26 Tesla in a clinical environment. Observations have been made on thigh muscles before and after exercise. This approach was based on the assumption that an increase of "free" water in muscles selectively exercised would permit the magnetization transfer technique to make an additional contribution to the enhanced image contrast known to occur between active and less active muscles (Fleckenstein et al, 1988).

Methods

The experiments were conducted on two normal untrained volunteers. MR images were obtained in the transverse plane using a Picker 0.26 Tesla superconducting whole body scanner. An MTC scan sequence was developed in which a saturation pulse was inserted immediately before a gradient recalled echo (GRE) sequence. The strength and duration of the pre-irradiation RF pulses were 6.2 μT and 96 ms, respectively (Fig. 1a). The corresponding GRE sequence was made compatible with the MTC sequence using the same scan parameters, but without the saturation pulse (Fig. 1b). The receiver gain for the input signal from the MTC sequence was set to the same db values as for the GRE sequences to permit comparison between the signal intensities within the same study. The saturation pulse was applied over a range of offset frequencies (−10 kHz to 10 kHz). Signal intensities (M) were measured in the presence (M_s) and in the absence (M_o) of saturation from circular regions of interest (ROI) from the vastus muscle group, the semimembranosus muscle group, the subcutaneous fat and the medullary cavity of adjacent bone.

Exercise was performed by knee flexion in the standing position for 1 min at a rate of 30 flexions/min. The thighs were re-scanned immediately after exercise. Sections scanned were marked on the skin to ensure the same location on each occasion.

The percentage increase in signal intensity after exercise was defined as:

$$M_{\%\text{increase}} = (M_{\text{post-exercise}} - M_{\text{pre-exercise}})/M_{\text{pre-exercise}} \times 100$$

The RF power deposition by the saturation pulse is proportional to its duty cycle (Bottomley & Edelstein, 1981). A range of repetition times (TR) from 500 ms to 300 ms was used. The maximum power deposition never exceeded 0.48 W/kg.

Results

A substantial signal loss was observed in all thigh muscles using pre-irradiation at the frequencies selected between −10 kHz to +10 kHz of the Larmor frequency

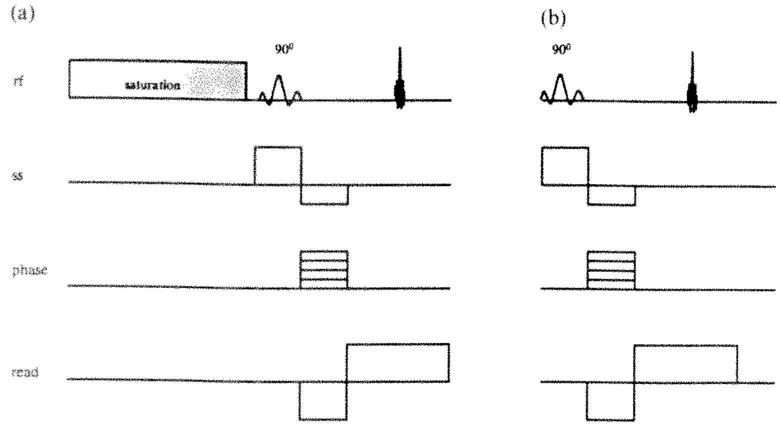


Figure 1. (a) MTC sequence and (b) GRE sequence.

of ^1H_f resonance. Figure 2 shows the ratio of the residual signal after saturation M_s and the signal without saturation M_o, *i.e.* M_s/M_o, plotted against the frequency offset of the saturation pulse using constant RF power. A significant decrease of M_s/M_o was observed in muscle over the whole range of frequencies used. No significant change was observed in fat and medullary cavity. The decrease of M_s/M_o in muscle is dependent on the pre-irradiation offset frequency. Data from the "free" water resonance with the irradiation $< +2$ kHz were not collected to minimize any effects of non-specific radiofrequency "bleeding over" (Wolff & Balaban, 1989). Figure 3 shows images with and without saturation. The images obtained with saturation demonstrate significant signal loss. After the flexion exercise, MTC images showed more signal difference between the vastus and the semimembranosus muscle groups, *i.e.* exercised and less exercised muscle, than observed previously. Figure 4 shows images with contrast changes before and after exercise. Signal intensity contrast between the active muscle group and the less active muscle group after exercise is more evident in the MTC images than in the images from the GRE sequences.

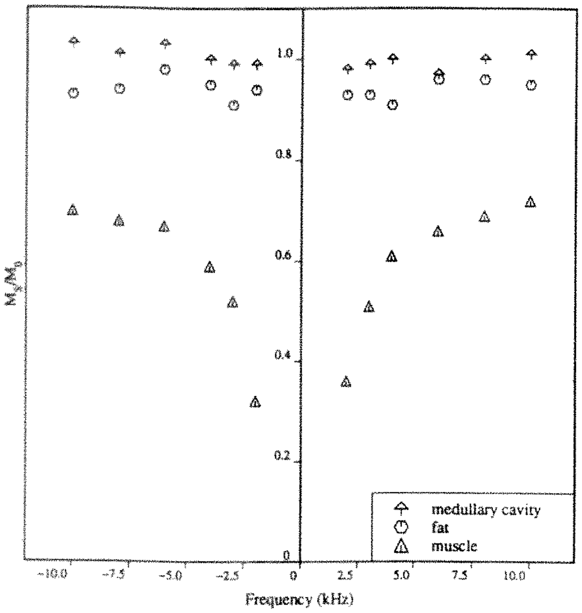


Figure 2. Effect of pre-irradiation frequency on the magnitude of the ^1H_f resonance of vastus muscle, subcutaneous fat and bone medullary cavity of adjacent femoral shaft from a healthy volunteer.

Table I shows signal intensities in arbitrary units of the vastus and semimembranosus muscles, measured from the MTC and conventional GRE images. There were no significant differences in signal intensity between the two muscle groups before exercise. After exercise the signal intensity of the more active vastus muscle group was significantly higher than that from the less active semimembranosus muscle group ($p < 0.05$) in

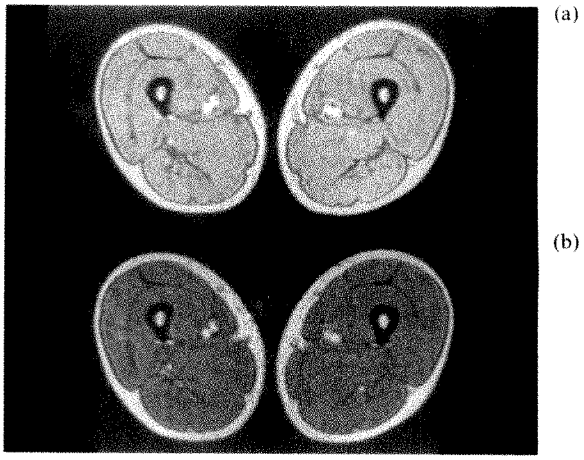
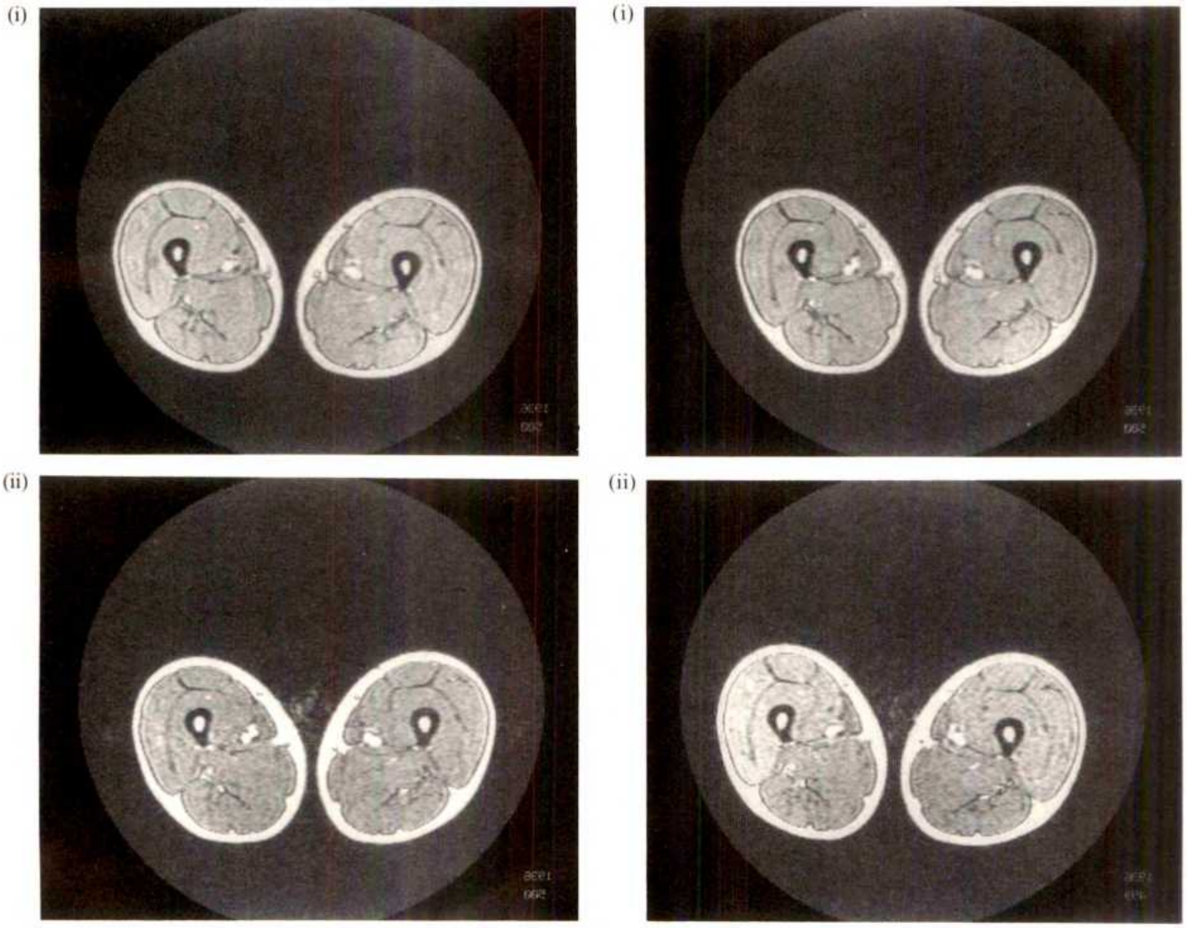


Figure 3. Transverse MR images of thighs from a healthy volunteer (a) T_1-weighted images using a GRE sequence with TR = 500 ms, TE = 18 ms; (b) MTC images with pre-irradiation. Frequency offset was 4 kHz followed by a gradient recalled echo collection with TR = 500 ms, TE = 18 ms; the images were obtained using the same db values of receiver gain and viewed with the same display window settings.



(a) (b)

Figure 4. Transverse MR images of thighs from a healthy volunteer (a) before and (b) after flexion exercise. (i) T_1-weighted images from gradient recalled echo sequences with TR = 500 ms, TE = 18 ms. (ii) MTC images with pre-irradiation. Frequency offset was 4 kHz, followed by a gradient recalled echo collection with TR = 500 ms, TE = 18 ms. The display conditions for the MTC 500 images which have undergone a significant signal loss have been adjusted to match the GRE 500 images.

Table I. Signal intensities in arbitary units measured from images obtained using saturation transfer and gradient recalled sequences in thigh muscles before and after exercise

	Muscle group		
	vastus	semimembranosus	t-test
	mean ± SD		
Before exercise			
GRE 500	956 ± 53	957 ± 53	$p > 0.05$
MTC 500	521 ± 43	508 ± 43	$p > 0.05$
MTC 2000	831 ± 48	834 ± 48	$p > 0.05$
After exercise			
GRE 500	1038 ± 36	992 ± 38	$p < 0.05$
MTC 500	664 ± 36	521 ± 31	$p < 0.001$
MTC 2000	1116 ± 86	851 ± 70	$p < 0.001$

the images obtained from conventional GRE sequences. Very significant differences in signal intensity were obtained from MTC 500 ($p < 0.001$) and MTC 2000 ($p < 0.001$) sequences. Whilst similar signal losses were observed in both muscle groups when the MTC sequences were used before exercise, the signal increase after exercise was considerably larger in the more active muscle group. Figure 5 illustrates the percentage increases in the signal intensities after exercise from MTC and conventional GRE sequences.

Discussion

MTC images obtained using saturation transfer techniques are believed to reflect the relaxation coupling or cross relaxation process between "free" water and water "bound" to macromolecules. The main limitation in the application of the saturation transfer method in human subjects is the large RF dose generated by the long

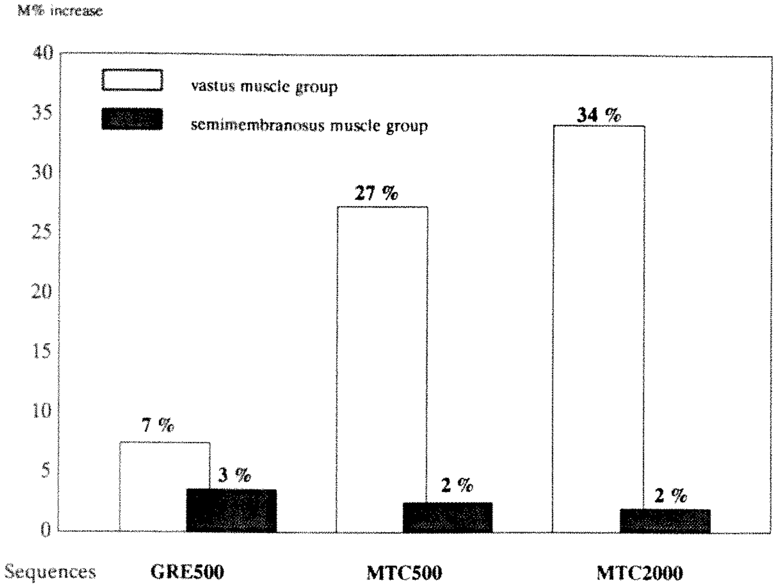


Figure 5. The percentage increases of signal intensities of the vastus and semimembranosus muscle groups after knee flexion exercise are shown for GRE and MTC sequences.

duration of the pre-irradiation pulse. This could become prohibitive at high field. The human studies conducted by Baudouin et al (1990) and Tanttu et al (1990) were carried out at very low field, 0.15 T and 0.1 T, respectively, using considerably shorter durations (50–300 ms) of the off-resonance irradiation RF pulse than the 3500–4000 ms originally employed by Wolff and Balaban (1989) in a high field small bore system. Selective saturation was nevertheless achieved and signal loss was observed in these human *in vivo* studies.

In this present study, experiments were conducted in a 0.26 Tesla (11 MHz) whole body scanner. The duration of off-resonance irradiation was limited to less than 96 ms and the duty cycle to less than 20% in order to guarantee an RF power deposition less than 0.48 W/kg, well below the safety guideline (1 W/kg) proposed by the National Radiation Protection Board (1983). Longer repetition times with a shorter duty cycle reduce heat deposition in the human body under strong RF irradiation (Bottomley & Edelstein, 1981). In our study a saturation pulse with a TR of 500 ms has also been tested to meet the preference of shorter scanning times required for clinical practice. The results suggest that the saturation transfer technique can safely be used at 0.26 T (11 MHz in frequency) with a range of repetition times from TR 500 ms to 3000 ms.

Dixon et al (1990) have demonstrated recently that the off-resonance irradiation occurring in day to day multislice imaging has a significant effect on signal intensity. Additional slices have been observed to reduce muscle signal intensity 10–20% in relation to fat. The RF strength and range of frequency offsets employed in the present study were similar to those recorded by Dixon et al (1990) but were of higher duty cycle. The RF irradiation used in the present study was approximately three times that of a typical spin echo multislice sequence, *e.g.* 15 slices (Fig. 2). Any clinical scanner with a multiple imaging facility could, therefore, be adapted to permit MTC experiments with larger signal reductions.

Signal intensity changes in muscle after exercise have been described by Young (1984) and Fleckenstein et al (1988). Fleckenstein et al reported an increase in the T_1 and T_2 relaxation times in exercised muscles. They attributed these changes to an increase in water, especially extracellular water content (Sjogaard & Saltin, 1982). The enhanced contrast observed in the present studies between active muscle and less active muscle in images with saturation irradiation can be attributed to this increase in extracellular water content. Despite a shorter duration of the saturation pulse compared with the experiments of Wolff and Balaban (1989), the MTC images obtained in this study still show significantly greater contrast between active and less active muscle groups. The results support their suggestion that an efficient magnetization transfer exists in skeletal muscle. The observations before and after exercise also suggest that magnetic transfer imaging may provide a more sensitive method to detect changes in water distribution in human skeletal muscle.

Conclusions

A significant contrast change has been observed in images obtained by a saturation transfer technique. Signal intensities of skeletal muscles were significantly suppressed with little change in subcutaneous fat or medullary cavity signals. After exercise selective saturation resulted in a significant increase of contrast between active muscle and less active muscle. The process of magnetization transfer in human imaging may provide new information about the exchange processes between "free" and "bound" water, processes which are related directly to the activity of macromolecules in biological tissue.

Acknowledgments

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The dependence of the scattered radiation dose to personnel on technique factors in diagnostic radiology

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Abstract. The measurement and prediction of scattered radiation dose to staff in diagnostic radiology is particularly important, owing to the increased use and complexity of interventional radiology. The air kerma–area product and scattered radiation dose in the vicinity of the patient couch, for both overcouch and undercouch X-ray tube geometries, were simultaneously monitored. The scattered radiation distribution at the couchside was deduced at a range of tube potentials for both overcouch and undercouch X-ray tube geometries. The variation of scattered radiation with field size on both geometries was investigated, as well as the variation with focus–table distance on an overcouch tube geometry. It was discovered that the scattered radiation dose at a point correlated with the air kerma–area product and the result may be used for radiation protection purposes. A method of predicting the scattered radiation dose at a given position is described.

The increasing use of interventional radiology has served to re-emphasize the general concern over staff exposures. The longer screening times involved imply a larger dose to staff. This may lead to some interventional radiologists with a high workload becoming classified radiation workers (*Ionising Radiation Regulations*, 1985). It is therefore important to be able to measure and predict the scattered radiation dose to staff arising as a result of X-ray examinations. Such knowledge would then enable staff doses for most types of examinations to be estimated from typical technique factors and the position of staff relative to the patient couch.

Scatter measurements and predictions of staff doses have been performed in the past (Faulkner & Moores, 1982; Jeans et al, 1985; Law, 1985; Palmer & Wright, 1985); however, all generally relate to specific equipment and examinations. It is difficult to interpret these results with any degree of precision for other units, even for units of the same make, because of variations in output and examination techniques. It is therefore important to measure scatter radiation on each unit. If, however, all fluoroscopic procedures are to be simulated, then the measurement and assessment of scattered radiation doses for each particular combination of technique factors becomes a time-consuming task. This paper presents a simplified method of assessing scattered radiation doses to personnel in diagnostic radiology and the results of a series of experimental measurements using this method.

A realistic patient-equivalent phantom (Rando Phantom, Alderson Research Labs, USA), was irradiated by both overcouch and undercouch tubes. The scattered radiation distribution around the Rando phantom was measured for X-ray beams at a range of tube potentials, together with the air kerma–area product monitored by a PTW Diamentor (Radiatron Components, Twickenham).

The objectives of this study were:

(1) To derive iso-air kerma curves for scattered radiation distributions for a range of tube potentials and field sizes, and for both overcouch and undercouch tube geometries.
(2) To find the dependence of scattered radiation on field size and Diamentor reading at various positions relative to the couch.
(3) To deduce the dependence of scattered radiation on tube potential at various positions relative to the couch.
(4) To discover the effect of focus–skin distance (FSD) on the scattered radiation distribution for several tube potentials at various positions relative to the couch on an X-ray unit with an overcouch tube geometry.

Materials and methods

The experiments were performed on a Picker Vector 70 microprocessor-controlled, three-phase, 12-pulse X-ray generator and a Picker PX401P X-ray tube. A Rando phantom was used to provide a source of scatter realistic of clinical practice. The phantom was laid in a supine position on the couch with the X-ray beam centred on the abdomen (slab 26) of the phantom.

Scattered air kerma was measured on a 25 cm grid in a plane parallel to the floor (see schematic diagram in Fig. 1). The air kerma measurements were performed using an 1800 cm^3 ionization chamber and an MDH 2025 dosemeter (Radcal Corp., Monrovia, California, USA). The ionization chamber was placed at a height of 100 cm above the floor, corresponding to the height at

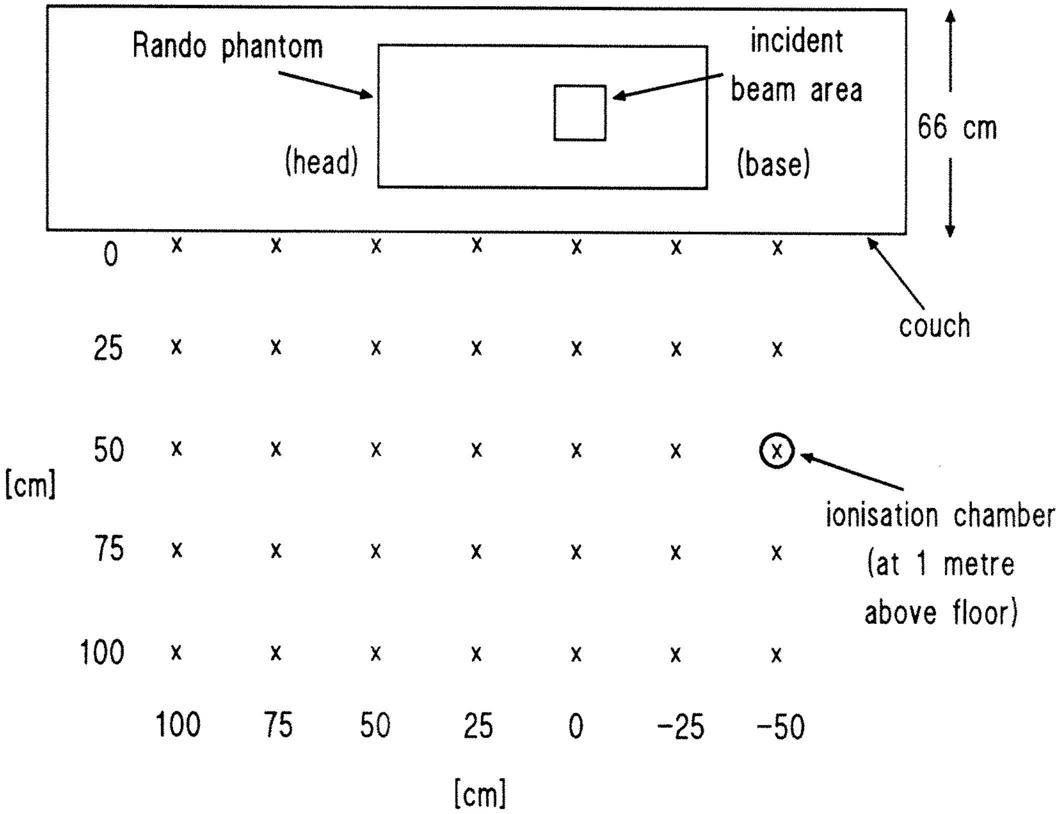

Figure 1. Schematic diagram of measurement geometry employed in this experiment. Measurements of scattered air kerma were made at the positions indicated by a cross, relative to the couchside.

which film badges are commonly worn. The calibration of the dosemeter employed was traceable to a National Standard.

Measurements were performed on the distributions of scattered radiation around the couch for a fixed field size (828 cm^2 and 434 cm^2 for overcouch and undercouch orientations, respectively) at nominal tube settings of 50, 70, 90 and 110 kV (200 mA, 100 ms) in radiographic mode. Measurements were repeated at certain locations to investigate the precision of the experimental technique. Scattered radiation produced by three further field sizes (473 cm^2, 181 cm^2 and 103 cm^2 for overcouch orientation and 250 cm^2, 102 cm^2 and 32 cm^2 for undercouch tube geometry) was investigated at a nominal tube setting of 90 kV (200 mA, 100 ms), again in radiographic mode. The accuracy of the tube potential settings was verified using a non-invasive potential divider. The various field sizes used were determined using a non-screen film (placed either at the entrance surface of the phantom when using an overcouch tube or on the underside of the table for the case of an undercouch tube) and the light beam diaphragm (LBD). The values found using these two methods were in agreement to within 2%. Iso-air kerma curves for the scattered radiation distribution (for the two tube geometries studied) were calculated through an interpolation technique based on the scatter values of a point of interest and its nearest neighbours.

The effect of FSD on the scattered radiation distribution adjacent to the couch was investigated (for overcouch orientation) by simply altering the distance of the anode from the Rando phantom and measuring the scattered radiation at positions in the vicinity of the couch. The measurements were performed for nominal tube potential settings of 50, 70, 90 and 110 kV (200 mA, 100 ms). Measurements were not performed to investigate the effect of varying FSD on an undercouch tube because the focus–table top distance on clinical equipment is generally fixed.

For each scattered radiation measurement the air kerma–area product was monitored. This was effected by the use of a calibrated Diamentor chamber (Radiatron Components, Twickenham) mounted on the tube housing. At a given tube potential, the Diamentor reading was used to correct for tube output variation. In the case of the undercouch geometry, an experimentally determined allowance for backscattered radiation onto the Diamentor chamber was made. A Bucky slot cover, also for this geometry, was simulated by placing a lead sheet in front of the X-ray tube.

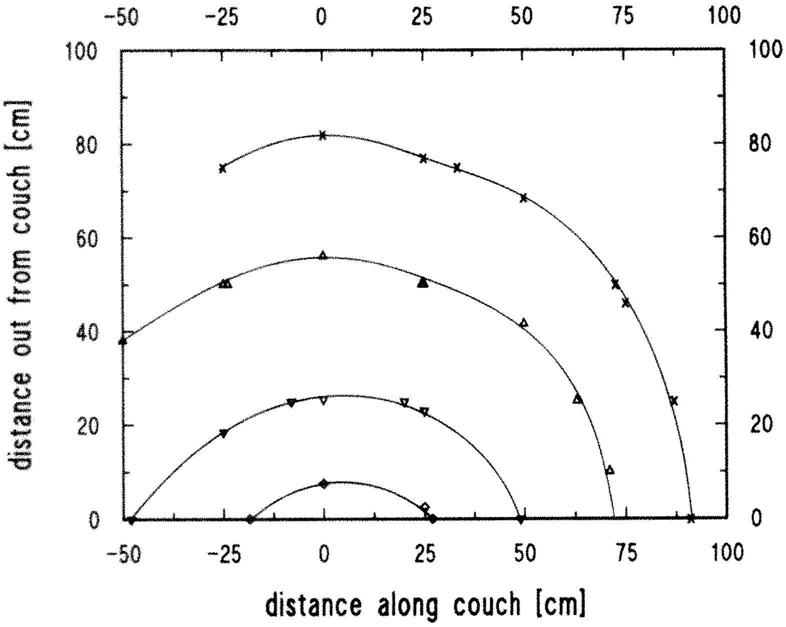

Figure 2. Iso-air kerma scattered radiation distribution measured at a height of 100 cm above the floor on an overcouch tube (90 kV, 20 mAs, 100 FCD). Field (828 cm^2) centred on slab 26 of a Rando phantom oriented with its head to the right (×, 6 μGy; △, 10 μGy; ▽, 20 μGy; ◇, 40 μGy).

Results

Iso-air kerma curves at a height of 100 cm above the floor are shown in Fig. 2 for a 90 kV beam with an overcouch X-ray tube geometry. All distances quoted are relative to the edge of the couch. A focus couch–top distance (FCD) of 100 cm was used, together with a field size of 828 cm^2 measured at the surface of the Rando phantom.

In Fig. 3, iso-air kerma curves are shown at a height of 100 cm above the floor for a 90 kV beam and an undercouch tube geometry. An FCD of 43 cm and a field size of 434 cm^2, as measured on the underside of the couch, were used.

Figure 4 shows plots of scattered radiation at various positions around the patient couch against Diamentor reading for four different field sizes irradiated using an

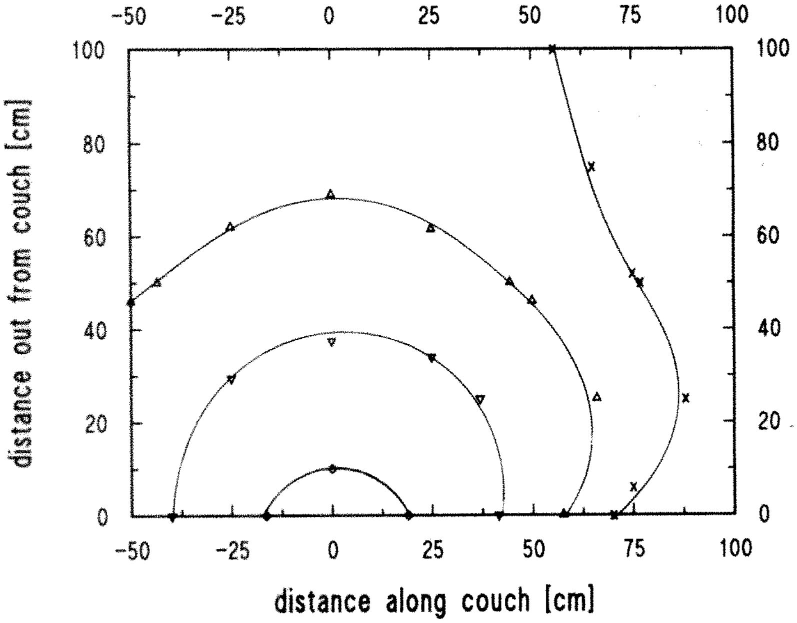

Figure 3. Iso-air kerma scattered radiation distribution measured at a height of 100 cm above the floor on an undercouch tube (90 kV, 20 mAs, 43 cm FCD). Field (434 cm^2) centred on slab 26 of a Rando phantom, oriented with its head to the right (×, 6 μGy; △, 10 μGy; ▽, 20 μGy; ◇, 40 μGy).

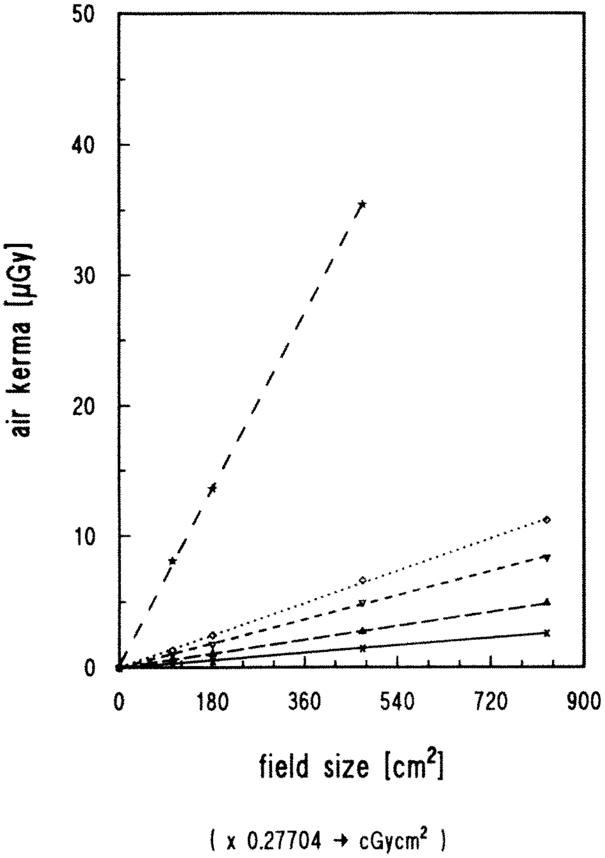

Figure 4. Variation of scattered radiation with field size for an overcouch tube geometry at five positions (90 kV, 20 mAs, 100 cm FCD). (★ (0,0); ◇ (0,50); ▽ (50,50); △ (100,0); × (100,100)).

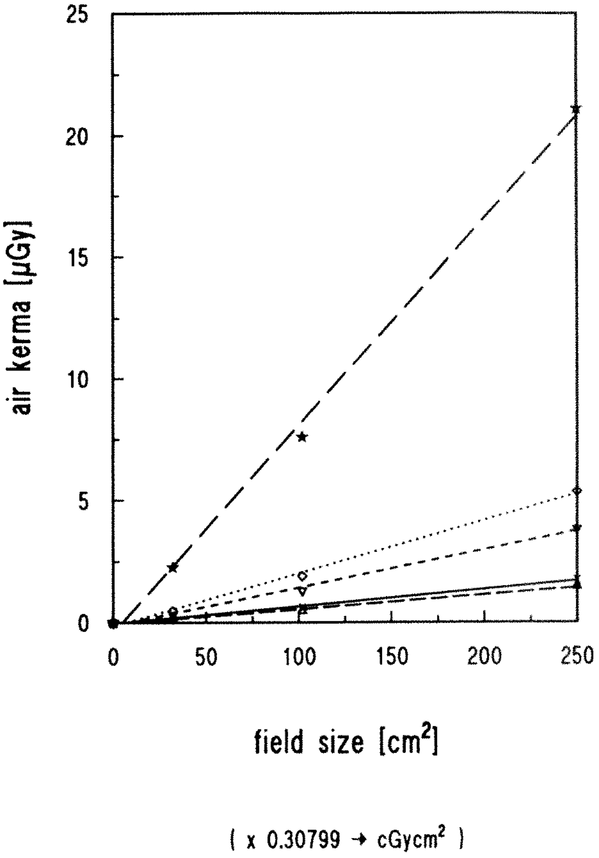

Figure 5. Variation of scattered radiation with field size for an undercouch tube geometry at five positions (90 kV, 20 mAs, 43 cm FCD). (★ (0,0); ◇ (0,50); ▽ (50,50); △ (100,0); × (100,100)).

overcouch geometry at 90 kV, 200 mA and 100 ms. Curves of scattered radiation against Diamentor reading for the same points, but this time for an undercouch tube (again at 90 kV, 20 mAs) and four different field sizes, are shown in Fig. 5.

The scattered radiation for different tube potentials at various positions adjacent to the couch, once normalized for output variations using the Diamentor reading, was investigated for both overcouch and undercouch geometries. Graphs of scattered radiation at various positions, plotted against tube potential for overcouch and undercouch geometries, are shown in Figs 6 and 7, respectively.

The effect of FSD on the scattered radiation was measured at various positions relative to the couch for tube potentials of 70 and 110 kV (20 mAs). The scattered radiation was independent of FSD to within ±6% (average error for all the points considered), at the two tube potentials investigated.

The precision of the measurements of scattered air kerma in this experiment was found to be 7% (standard deviation expressed as a percentage of the mean). The anticipated accuracy in the positioning of the dosemeter leads to a typical uncertainty of ±5% in the measured amount of scatter. The estimated accuracy of the calibration factor of the ionization chamber is ±5%. The methods used for estimating field size (*i.e.* direct measurement using the LBD and measurement using film) were found to agree to within 2%. There are two further uncertainties pertinent to the iso-air kerma scattered radiation distributions (shown in Figs 2 and 3). The first of these is due to the interpolation technique used to deduce these curves, which could be as high as 10%, and the second is the accuracy of the calibration factor of the Diamentor, which is ±3%. These uncertainties result in an overall error of approximately 13% on the data presented in Figs 2 and 3.

In Figs 4 and 5, the overall uncertainty is less (because no interpolation technique was used) and is thought to be approximately 8%. The uncertainty on the measure-

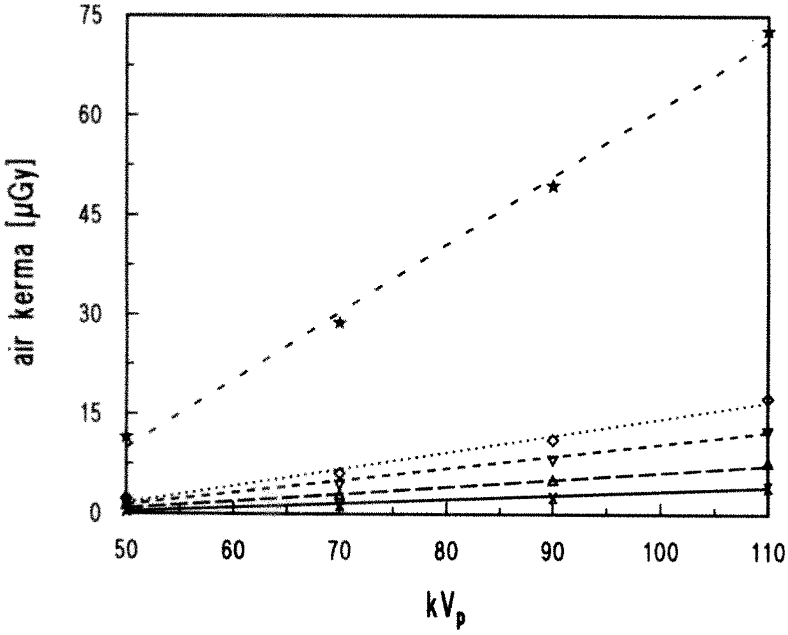

Figure 6. Variation of scattered radiation with tube potential for an overcouch tube geometry at five positions (828 cm^2 field, 20 mAs, 100 cm FCD). (★ (0,0); ◇ (0,50); ▽ (50,50); △ (100,0); × (100,100)).

ments presented in Figs 6 and 7 is slightly higher owing to the accuracy of the tube potential calibration of ±3 kV.

Discussion

The iso-air kerma curves presented in Figs 2 and 3 are not symmetric and a number of factors may have given rise to this. The non-uniform composition of the realistic phantom will perhaps have the most significant effect on the symmetry of the scattered radiation. Other factors that could affect the shape of the curves will be the geometry of the room and tube-leakage radiation. It was anticipated that the effect of backscatter from the walls would be small and this was later confirmed experimentally. In addition, the leakage radiation was measured and found to be negligible. As can be seen from these figures, the scattered radiation associated with an undercouch tube geometry is substantially lower

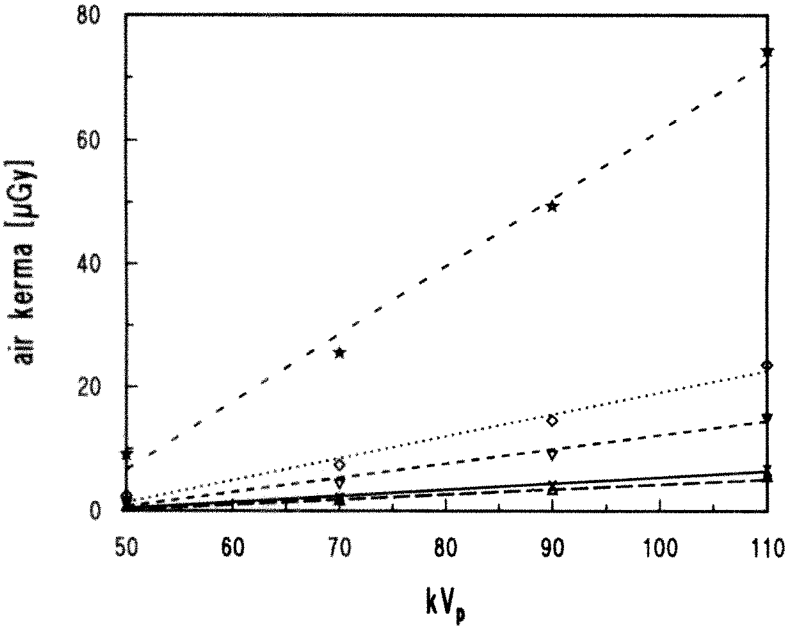

Figure 7. Variation of scattered radiation with tube potential for an undercouch tube geometry at five positions (434 cm^2 field, 20 mAs, 43 cm FCD). (★ (0,0); ◇ (0,50); ▽ (50,50); △ (100,0); × (100,100)).

than that produced with an overcouch tube, when allowance is made for the difference in field size at the entrance surface of the phantom and FSDs.

It may be deduced from Fig. 4 that, for a range of field sizes and for the phantom used in this investigation, the scattered radiation at a point (for a given tube potential) is directly proportional to the field size (and thus the Diamentor reading), to within an accuracy of approximately 5%. This observation also applies to the plot of scattered radiation against Diamentor reading for an undercouch tube, shown in Fig. 5. For this tube orientation, however, the proportionality only holds to within about 15%.

It may be surmised from Figs 6 and 7 that tube potential has an effect only on the value of air kerma to which each iso-air kerma curve refers and has little effect on the shape of the distribution of the scattered radiation. The magnitude of the scattered radiation at a point was found to be proportional to the variation in measured air kerma–area product (cGy cm^2) with tube potential. This proportionality then enables the measurement of air kerma–area product (cGy cm^2) and scattered air kerma at one tube potential and a given position to be used to predict the scattered radiation for different technique factors (but at the same tube potential and position) to within an uncertainty comparable to the anticipated experimental accuracy. When the scattered radiation at one tube potential is used to predict the scattered radiation at another tube potential (within ±20 kV), then the estimated scatter was found to agree with the measured value to within 10% for overcouch geometry and to within 20% for undercouch geometry.

For an overcouch tube geometry, changing the FSD by almost a factor of 2 had very little effect on the distribution of scattered radiation at a given position relative to the couch.

The data presented in this paper for overcouch tube geometries may be compared with scattered radiation distributions published by other authors (Hoffmann et al, 1971; Stacey et al, 1974; Palmer & Wright, 1985; Hemmingsson & Lofroth, 1978; Faulkner & Moores, 1982). Unfortunately, it was not possible realistically to compare the results presented here for an undercouch tube geometry with previously published work, owing to the differences in measurement position and X-ray equipment. The comparison for an overcouch tube geometry has been performed for various positions, at the couchside and 100 cm away. The scattered radiation data presented here may be corrected in accordance with our findings on the variation of scattered radiation with tube potential, tube output and field size. For overcouch X-ray tubes, the corrected data agreed with the previously published data, typically within 20%. The maximum difference, however, between the corrected and original data was approximately 70%. This comparison underlines the usefulness of the extrapolation method we have outlined.

The method of predicting the scattered radiation at a point from a combined measurement of scattered radiation and air kerma–area product at different technique factors can also be implemented if a Diamentor is not available. This can be achieved by measuring the tube output with a dosemeter and the field size (*e.g.* using a film) at the chosen point. The air kerma–area product can then be calculated from these measurements.

Conclusion

These results imply that, for a given position, the scattered radiation at that position correlates with the air kerma–area product measured at the X-ray tube housing, irrespective of the tube potential and field size for both undercouch and overcouch geometries. This result has an important consequence in the prediction of staff doses. A base measurement of the scattered radiation at the position of interest should be made at the required tube potential, along with the air kerma–area product registered by a Diamentor. The scattered radiation at this position (for further exposures at different technique factors) can then be predicted by scaling this base reading of scattered radiation in accordance with the air kerma–area product measured for different field sizes and tube potentials. The effect of FSD on the predicted value has been shown to be negligible. This base measurement can also be used to estimate the scattered radiation, for tube potentials within ±20 kV of the baseline measurement, to an accuracy of 10% for an overcouch geometry and 20% for an undercouch geometry.

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Improved image quality for dense breasts in mammography

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Abstract. Within the UK breast scanning age range of 50–65 years, about 15% of breasts show a dense structure that is underexposed in conventional mammography. This gives rise to a severe reduction in contrast. Methods of improving this contrast by variation of exposure factors are explored, using a Dupont phantom that has a simulated dense breast structure. Results are assessed by considering measured contrast from a Perspex stepwedge, and by obtaining relative scores, on a scale of 1–10, from 15 radiologists involved in mammography. It is concluded from both these methods that approximately doubling the mAs at the normal kV is preferable to increasing the kV by more than a small amount. A modified mammographic technique on these lines could be valuable in selected cases where a previous conventional mammogram was available, i.e. assessment stage or repeat screening in a screening programme, or symptomatic patients. Practical problems in choosing exposure factors and the magnitude and implications of the increased dose are discussed.

In the breast screening age range as currently defined in the UK, i.e. 50–65 years, about 15% of mammograms show a dense structure extending over an area of about 10 cm^2 or more. At younger ages the percentage may be greater. These structures give rise to pale areas on the mammograms, so that the general film density level is well below the linear portion of the characteristic curve of the film–screen combination. As a consequence of this, the degree of contrast (i.e. change of density for a given exposure ratio) within these areas is relatively low, corresponding to the reduced slope of the characteristic curve (Fig. 1), and in the photographic sense these areas are underexposed.

In this paper, radiographic contrast, C, is used in the conventional sense of the term, as the difference in optical densities D_1 and D_2 of adjacent areas on the film, *i.e.* $C = D_1 - D_2$. Since the characteristic curve for the response of a film–screen combination is plotted with exposure on a logarithmic scale, it follows that on the straight line portion of that curve, contrast is proportional to a given exposure ratio for adjacent areas.

The degree of contrast that can be obtained would be increased if the film density level were increased, and would be maximized if the density level were raised sufficiently to bring it within the linear portion of the characteristic curve. This might be achieved by an increase in exposure (mAs), or by an increase in X-ray tube potential (kV). Darker mammograms would have certain advantages. Fewer dense structures would be underexposed so that more films would give optimum

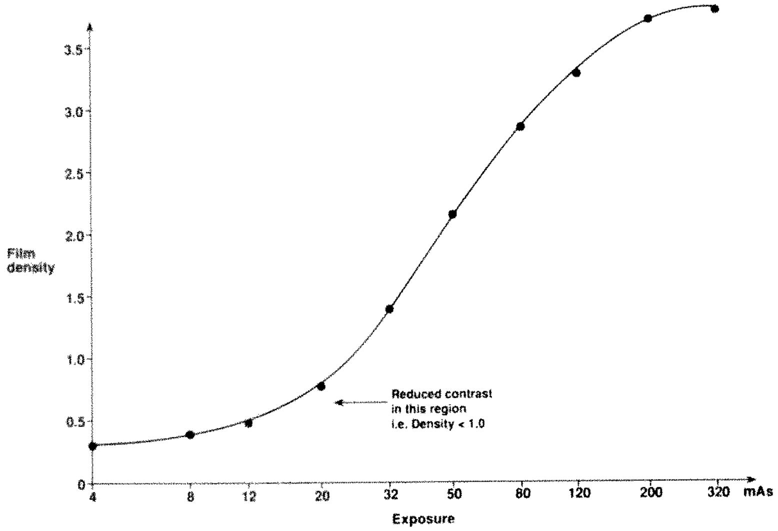
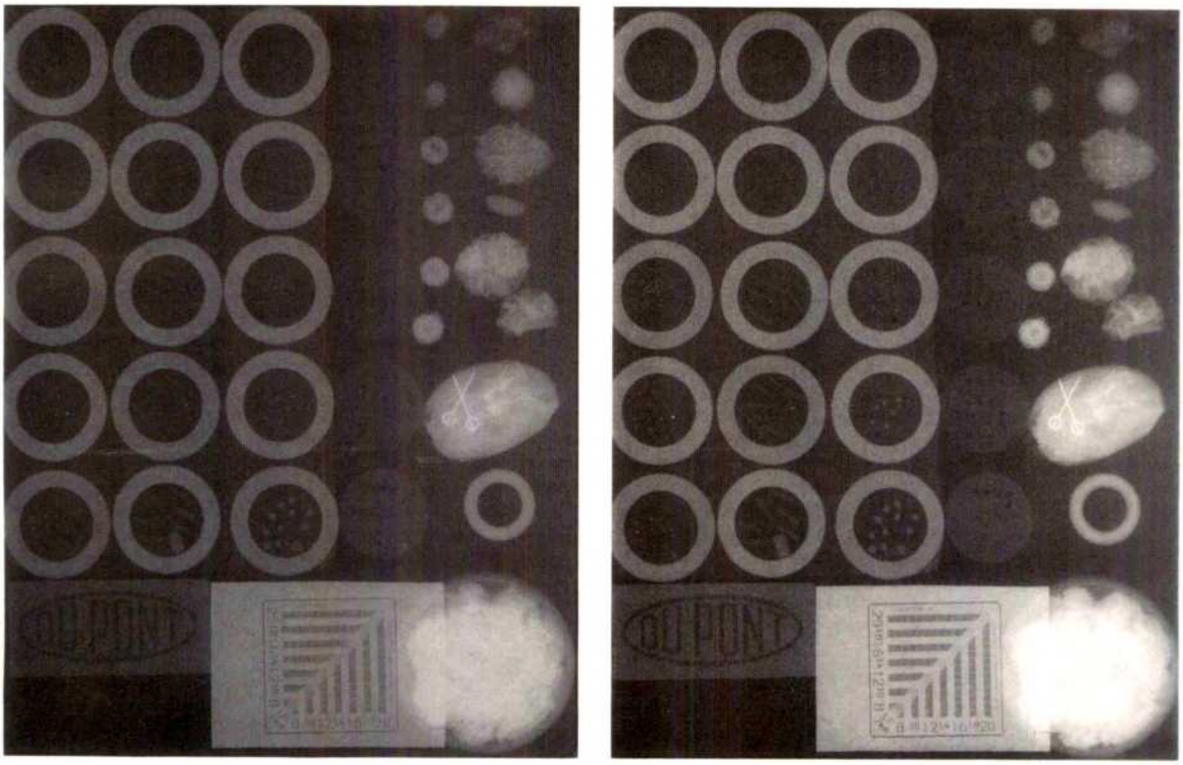


Figure 1. Characteristic curve for Fuji MA film with Fuji Fine screen.



(a) (b)

Figure 2. Phantom showing dense structure (lower right). (a) Normal exposure: 28 kV, 63 mAs. (b) Increased exposure: 28 kV, 120 mAs.

contrast over their whole area. Also, they would be less susceptible to sudden falls in processor speed index, as are occasionally observed in a quality assurance (QA) programme. There are also disadvantages. Increasing mAs increases dose and may also lead to less dense structures (e.g. skin outline) becoming overexposed, while an increase in kV has the potential for reducing contrast, and if the kV is raised sufficiently this will outweigh any gain from the characteristic curve.

The purpose of this paper is to investigate both methods of increasing film density and to assess which technique is likely to be preferred by radiologists. The practical implications and possible applications of the conclusions will also be discussed.

Method

In order to obtain suitable mammograms under a variety of exposure conditions it was necessary to use a phantom having at least one feature that simulated a dense breast structure. The possibility of experimenting with exposure conditions in a series of clinical mammograms was rejected. Even if such an approach were acceptable in symptomatic patients, the structures in each breast would be too varied to allow sufficiently close comparison between the films.

The phantom chosen was the one produced by DuPont (Law, 1991a). This contains one circular feature approximately 2 cm in diameter, made of organic material with calcifications, which simulates a dense breast structure (Fig. 2, lower right). For the present work the phantom block carrying all the test details seen in Fig. 2 was placed above a 3 cm Perspex slab and beneath another 1 cm Perspex slab, with a Perspex stepwedge alongside having 5 mm steps. This arrangement is that recommended for this phantom by its makers. The total phantom thickness was equivalent to a compressed breast thickness of about 5.5 cm, slightly greater than the average quoted in IPSM (1989) but close to the average observed in Scotland (Law, 1991b). In the subsequent film analysis, film densities measured under the first five steps of this wedge were considered, along with images of the simulated dense breast. The numerous other test details in the DuPont phantom were ignored in this work.

Films of the DuPont phantom were taken on a CGR 600T mammography X-ray set in the Edinburgh Breast Screening Centre. This set has a three-phase generator and a molybdenum target with 0.03 mm molybdenum filter. Films were taken with the phantom placed directly on the grid cover and under compression, and with the cassette in its usual place below the grid, i.e. in contact film geometry. The broad focus was used, the nominal size being 0.3 and the actual size as measured by slit and star pattern on several occasions averaging

0.37 mm × 0.50 mm. The tube voltage was set at 28, 31 or 33 kV; the actual kV was checked by fluorescence and found to be lower than the nominal value by an amount less than 0.2 kV. An electronic kV meter (model 232 from Gammex RMI) suggested a small error in the same direction, possibly up to 0.9 kV, but the fluorescence results are considered to be the more reliable.

The film was Fuji MA, with Fuji Fine screens in Fuji cassettes, this being the system at present in use in the Edinburgh Centre. The processor was a DuPont T5A, with Tetenal chemistry, running at 35°C and 2.5 min dry to dry.

An initial film of the phantom was taken under automatic exposure control and required approximately 60 mAs. The X-ray set was then switched to manual control and the nearest mAs setting of 63 was used for three films, one in each of three cassettes. One of these is shown in Fig. 2(a). The density level under the dense breast structure was approximately 0.45 and varied only within about ±0.02 as the densitometer was moved within the area of this structure. Such a small variation might be expected for simulated breast tissue over distances of around 1 cm. Thus the density level lies well down the characteristic curve as expected. Three more films were then taken in the same three cassettes at 120 mAs, and a further three at 160 mAs, all at the same 28 kV. One film at 120 mAs is shown in Fig. 2(b). The corresponding density levels under the dense structure were 1.00 and 1.37. The first of these is just within the linear portion of the characteristic curve, and the second is well within the linear portion.

Further sets of three films were obtained, also in the same cassettes, using 31 kV and 33 kV, and all at the original 63 mAs. These gave dense structure densities of 1.03 and 1.51, respectively, broadly similar to those from the films at 28 kV and increased mAs. All 15 films were exposed and processed within about 1 h.

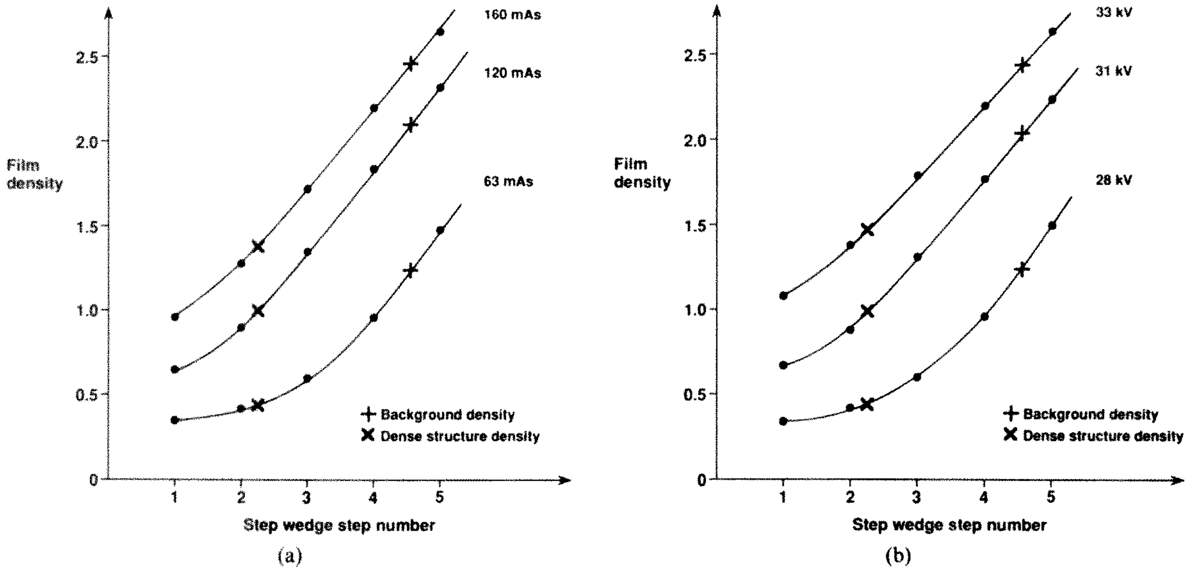
Results

Analysis of stepwedge densities

In a separate investigation the characteristic curve of this film–screen combination was established by exposing successive strips of a single film in a cassette to progressively increased X-ray exposures (Fig. 1). This confirmed that the straight line portion of the characteristic curve did not begin below a density of 0.8 and was only clearly established above 0.9. Other films (e.g. Kodak OM1) are similar.

Measurement of film density beneath the stepwedge in each of the 15 films agreed with this. The results are given in Table I and plotted in Figs 3(a) and 3(b). It is assumed for purposes of graph plotting that the exposures beneath successive steps increase uniformly on a logarithmic scale. This is consistent with the characteristic curve in Fig. 1, and is reasonable if it is supposed that there is no appreciable net beam hardening under successive 5 mm layers of Perspex. Even if this assumption is not correct it does not affect later conclusions.

A detailed analysis of Table I and Figs 3(a) and 3(b) shows that at 28 kV the difference in density between successive steps of the wedge other than the first shows negligible change between 120 and 160 mAs, whereas at 63 mAs the same contrast is only reached for the fourth and fifth steps. The general density level beneath the dense structure is consistently slightly greater than that of the second Perspex step. This implies that the small contrasts within the dense structure are not increased by increasing exposure beyond 120 mAs. The film density in the background to the other details of the phantom was always about midway between the fourth and fifth



(a) (b)

Figure 3. Densities under stepwedge in phantom films. (a) 28 kV, various mAs; (b) 63 mAs, various kV.

Table I. Mean densities under steps of Perspex wedge

Exposure factors		Step number					Dense breast structure	Background area
kV	mAs	1	2	3	4	5		
28	63	0.34	0.41	0.60	0.97	1.49	0.45	1.25
28	120	0.65	0.89	1.36	1.84	2.33	1.00	2.10
28	160	0.96	1.27	1.72	2.20	2.66	1.37	2.46
31	63	0.67	0.89	1.33	1.78	2.23	1.03	2.05
33	63	1.09	1.39	1.80	2.20	2.63	1.51	2.47

Table II. Results of scoring of dense breast image by 15 radiologists

Exposure factors		Mean score	Departure from each radiologist's mean for 12 darker films with standard error (68% confidence level)	
kV	mAs			
28	63	2.40±0.23	—	
28	120	7.15±0.23	+0.44	±0.22
28	160	7.23±0.32	+0.52	±0.17
31	63	6.73±0.22	0	±0.12
33	63	5.57±0.20	−1.07	±0.19

steps, and well within the straight line region, even at 28 kV and 63 mAs.

For the films taken at 31 and 33 kV, a similar inspection of the stepwedge densities and the differences between them shows a reduction in contrast in the 31 kV films compared with those at 28 kV, and similar reduction in contrast in going from 31 to 33 kV. These results suggest a provisional conclusion that, of the four sets of films at increased densities, those at 28 kV are slightly to be preferred over those at 31 kV, with those at 33 kV being more distinctly inferior. An increased exposure, either doubling mAs at 28 kV, or increasing by 3 kV without changing mAs, might be necessary.

Assessment by radiologists of dense structure images

A number of consultant radiologists in the Scottish Breast Screening Programme assessed the films, as did two visiting radiologists from England and Italy, the total number being 15. These included some with many years experience of reading mammograms, others who joined the screening programme at its inception and others who joined very recently or have yet to start. Each radiologist was told initially how the three films at 28 kV and 63 mAs had been obtained and that the other 12 had been given a variety of different exposures all designed to produce darker films with greater contrast. They were then asked to "score" the films on a scale of 0–10, considering only the image of the dense structure. They were encouraged to look at all 15 films fairly quickly and then consider each film more slowly before writing down any scores. No time limit was set and all took between 10 and 20 min. Scoring was completely independent between each radiologist and took place on a number of occasions over several weeks and in four different screening centres. After the first three radiologists' scores were known, each of the remaining 12 were told that previous scorers had generally given between 1 and 3 to the films at 28 kV, 63 mAs, and between 5 and 9 to the other 12 films. (This information was given to them in order to assist their familiarization with the films and thus save their time.) This pattern of scoring was broadly maintained, with a very few exceptions. No radiologist knew the factors for any of the 12 darker films, or that they were grouped in four sets of three.

The radiologists found the simulated dense breast structure to give a fair representation of the appearance of dense structures seen in mammograms.

The mean scores for each group of three films, for all 15 radiologists, are given in Table II. The differences between the second, third and fourth groups appear rather small, and are not statistically significant.

Table III. Merit order of each radiologist's scores for 12 darker films

Exposure factors		Number of radiologists placing			
kV	mAs	1st	2nd	3rd	4th
28	120	8	2	3½	1½
28	160	7	3	5	0
31	63	0	8	5½	1½
33	63	0	2	1	12

Note: Half entries arise from one radiologist placing two groups 3rd equal.

However, the results can be assessed in other ways. Ignoring the low-scoring pale films, the mean score for each radiologist was calculated from the 12 darker films. The range of these means was 5.3–8.1. For each group of three films and each radiologist, the difference from that radiologist's mean was taken, and the average of these differences with their standard errors (68% confidence level) was then calculated. These values are given in the next column of Table II under "departures from means", and the differences in scoring are now increased, though the second and third groups of films, those at 28 kV with increased mAs, still score almost equally. The result at 31 kV now appears inferior to those at 28 kV, although the statistical significance of the difference is not large ($p < 0.05$).

Another, and more revealing, approach is to consider the merit order given by each radiologist to the four groups of darker films. This is shown in Table III. All 15 radiologists gave their highest scores to one of the two film groups at 28 kV, but opinion was fairly evenly divided between the 120 and 160 mAs groups. Second choices were concentrated more on the group taken at 31 kV, but greatest consistency was shown in scores for the 33 kV films, which were rated lowest of the four by 12 out of 15 radiologists. These results are plainly not due to chance ($p < 0.0001$), and a formal statistical test scarcely seems appropriate in this instance. A clear preference for 28 kV rather than 31 or 33 kV has been established.

Many of the radiologists, especially those with least experience, commented that they found it quite difficult to decide between the best three of the groups of darker films, and some added that they would accept films under any of those conditions. In view of these remarks, the consistency of their preference for 28 kV is perhaps more noteworthy.

A more detailed breakdown of scores showed no detectable difference in merit order placing between very experienced and the least experienced radiologists. There was no significant difference in scoring between the three cassettes when all the films on each were averaged, but there were occasional slight differences between single films within a group of three. For example, one of the three initial pale films was given a higher score than one or both of the other two by 12 radiologists out of 15. This implies a high degree of consistency between different radiologists, again regardless of degree of mammography experience.

Discussion and conclusions

Both the scoring by radiologists and the stepwedge results suggest that improved imaging of dense breast structures is more readily achieved by increasing mAs at the normal kV (in this case 28) rather than by increasing kV. For breasts of around average thickness, any kV increase should not exceed 3 kV, though that figure might be slightly greater for very thick breasts, and slightly smaller for very thin ones. For the average breast, a smaller increase in kV would need some compensatory increase in mAs.

Radiologists with experience in mammography seem to be generally agreed that it is impossible to know whether a dense structure is present in a breast until a film is obtained. There is therefore no question of modifying technique at an initial screen. A modified technique could have a useful role in selected cases in three other circumstances:

(a) those recalled for assessment from the initial or later screens,
(b) those undergoing a second or later screen, assuming films from the first screen were looked out and checked in advance, and
(c) symptomatic patients.

In all three groups it would be for the radiologist to select those cases in which a darker film would be desirable and advise the radiographer accordingly.

There may be practical problems over choice of exposure factors. Almost all mammographic exposures are now made under automatic exposure control (AEC). Thus to get a single exposure at (say) double the normal mAs, or at the same mAs but a higher kV, the AEC control would need to be substantially adjusted; for example, on the Siemens Mammomat 2 the adjustment needed is +3.0. Other models of X-ray set may have an inadequate range of adjustment. Alternatively, a note may need to be made of the original mAs and manual exposure used at the setting nearest to or next above double that value. If a change of kV is preferred, the manual alternative may be the more reliable. It will be important to revert to routine procedure before the following films are taken. Making two identical exposures under AEC within a few seconds carries the risk that, even under compression, the breast may move, and on some X-ray sets it is not possible in under 30 s.

A more practical procedure therefore may be to note the mAs from an exposure under AEC at the usual kV, and then to obtain the darker film by using the nearest manual mAs setting to double that amount and at the same kV. It would be advisable to go to the next highest available setting rather than the next lower one. Alternatively, the nearest manual mAs setting to the mAs delivered under AEC might be used with the tube potential increased by 3 kV. Either procedure is facilitated by keeping a written record of kV and mAs (and any fine tuning of AEC control) for every mammogram taken. This is already routine in many centres. X-ray sets having manual mAs settings in steps of approximately 10% rather than 20–25% also present some advantage.

Unless the dense structure is the only feature to be considered in the mammogram (which is very uncommon), a film dark enough for the dense structure may be too dark for many other features, especially for example the skin outline. Use of a "brightlight" may overcome that problem, and this might be acceptable provided the number of films that required it in a reporting session was not excessive. It is possible that the dark film would be taken in addition to one under normal exposure factors, notwithstanding the extra dose required. This underlines the need for selection by the radiologist of appropriate cases.

For a film taken at 28 kV with double the normal mAs the patient dose is also double the normal. For a film at 31 kV but normal mAs, the surface dose will be approximately 40% greater than normal but there will be a further increase in mean breast tissue dose because of the increased penetration, and the resulting overall increase to breast tissue will be around 50% (IPSM, 1989). Doses in mammography are at present approximately 1 mGy per film to breast tissue or 5 mGy to skin (Law, 1991b). At this dose level, and with typical cancer detection rates of over 5 per 1000 examinations, the ratio of the number of cancers detected to the number that might be induced is at least 200 to 1 at initial screen even if two films are taken per breast, and nearly as large at subsequent screening after only a 2-year interval (Law, 1987). The current 3-year interval will increase that ratio. These ratios are large, and support the view that, at these dose levels, maintaining or improving image quality is more important than dose reduction, desirable though that is in itself. Therefore a doubling or even trebling of dose appears acceptable in selected cases, provided always that it is accompanied by a significant increase in image quality and a reasonable prospect of useful additional diagnostic information being obtained.

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A standardized multifield irradiation technique for breast tumours using asymmetrical collimators and beam angulation

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Abstract. Combined angulation and asymmetrical collimator matching techniques are used for field alignment in breast irradiation. A local regional irradiation technique has been developed that allows a uniform dose distribution to the entire target volume. The localization is characterized by simple measurement of a few patient co-ordinates. The equipment settings to produce a theoretical exact field alignment are calculated by a special computer program. These settings guide the simulation. We have designed the method such that the technique is standardized for all patients receiving breast and lymph node irradiation. This allows an easy, accurate and fast patient throughput at the simulator and accelerators.

Because of its number and complexity, breast cancer irradiation forms a significant load at radiotherapy departments. Breast irradiation techniques, particularly those where the breast and draining lymphatics are to be encompassed, are characterized by complex three-dimensional field matching problems. Opposing tangential fields covering the breast must be aligned with a supraclavicular field, one or two axillary fields and occasionally with an internal mammary chain field. The field matching in existing irradiation practice is often limited to some field alignment using the simulator light, making overdosing (up to 200%) and/or underdosing, because of beam divergence, unavoidable (Svensson et al, 1980). It is essential that all fields geometrically match to ensure both local control and good cosmetic results. Advanced field alignment techniques described in the literature use partial blocks, fixed (Lebesque, 1986) or gravitationally positioned (Svensson et al, 1980), half-beam blocks (Podgorsak et al, 1984; Siddon et al, 1981), or combinations of both (Lichter et al, 1983; Siddon et al, 1983). Field matching techniques for multifield breast irradiation avoiding the use of cumbersome block techniques have been developed by Casebow (1984), using the angulation techniques described by Fleming and Orchard (1974), Casebow (1976) and Siddon (1981). This paper can be considered as a further development of these techniques using combined angulation and asymmetrical collimator matching techniques. A lymph node irradiation technique has been developed that allows uniform 50 Gy irradiation to the entire target volume. Localization is by simple measurement of a few patient co-ordinates. The equipment settings to produce a theoretically exact field alignment are calculated by a special computer program. These settings guide the simulation.

We have designed the method so that the technique has been standardized and can be applied to all patients who are considered for irradiation of the breast, thoracic wall and regional lymph nodes. This technique allows an easy, accurate and fast patient throughput at the simulator and accelerators.

Requirements

The basis of our irradiation technique is shown in Fig. 1. The goals for the tangential fields are as follows: (i) a uniform dose distribution (within 5% of the dose maximum) in the whole breast or thoracic wall; (ii) a skin dose of approximately 70% of the prescribed dose when breast conserving therapy is performed and 100% in the case of a modified radical mastectomy; (iii) minimal radiation dose to the lung; (iv) a uniform dose match at the supraclavicular and axillary fields at all depths; and (v) a reasonable dose match to the parasternal field. Moreover, the tangential fields must aim to eliminate the effect of breast volume and breast position on dose distribution and field matching accuracy.

The prescribed dose must be given to the supraclavicular nodes, which are about 3 cm from the skin, and to the axillary nodes, which reach the mid-axillary level or even deeper. Because the proposed dose to all regional lymph nodes is 50 Gy in 25 fractions, 5 fractions a week, dose inhomogeneities, which can result in unacceptable fibrosis, should be avoided.

When a parasternal field is used it must cover the homolateral internal mammary chain to a depth determined by the distance from the skin to the dorsal side of the deepest-located retrosternal lymph node.

All fields must match each other in such a way that

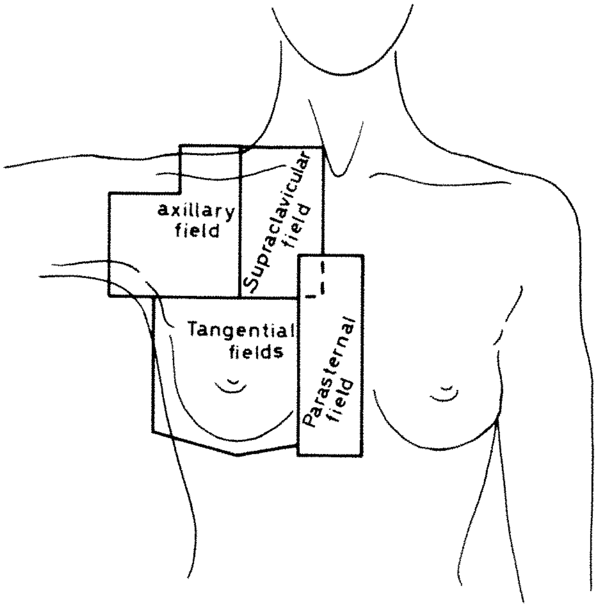

Figure 1. Basic scheme of the irradiation technique.

dose inhomogeneities are avoided and irradiation damage to normal tissue is prevented.

Field matching

One match plane

In order to match two fields according to the parallel field alignment, two basic techniques can be used. First, the penumbra of the fields can be enlarged by using a match-line wedge (Fig. 2a) and secondly, non-diverging field sides can be made that match at the skin. The plane in which the fields are to match is defined as the match plane (Fig. 2). Match-line wedges diminish the dose inhomogeneity, with the result that the field positioning is not critical (Fraass et al, 1983). The non-diverging fields can be obtained using half-beam blocks or asymmetrical collimators (Fig. 2b) or angulation techniques (Fig. 2c). When using these techniques in the parallel field situation they are characterized by extreme homogeneous but critical matching. Small misalignments do produce large dose inhomogeneities.

If the fields are matched according to the situation of the opposing field alignment of Figs 2d and 2e, easy non-critical matching is obtained with both non-diverging field techniques.

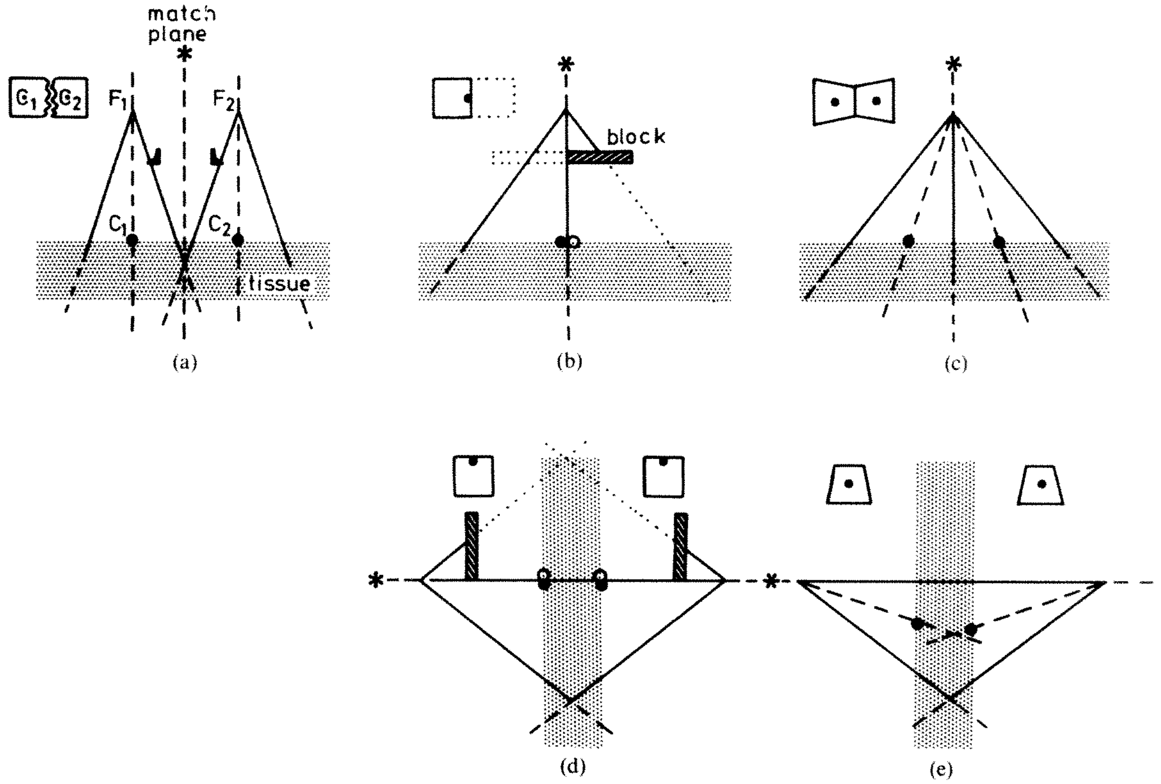

Figure 2. Parallel field alignment using match-line wedges (a), the half-beam technique (b) and the angulation technique (c). Opposing field alignment with the match plane using the half-beam technique (d) and the angulation technique (e). C1 and C2 indicate the field central axis. The insets give the field size and field deformation at the skin surface.

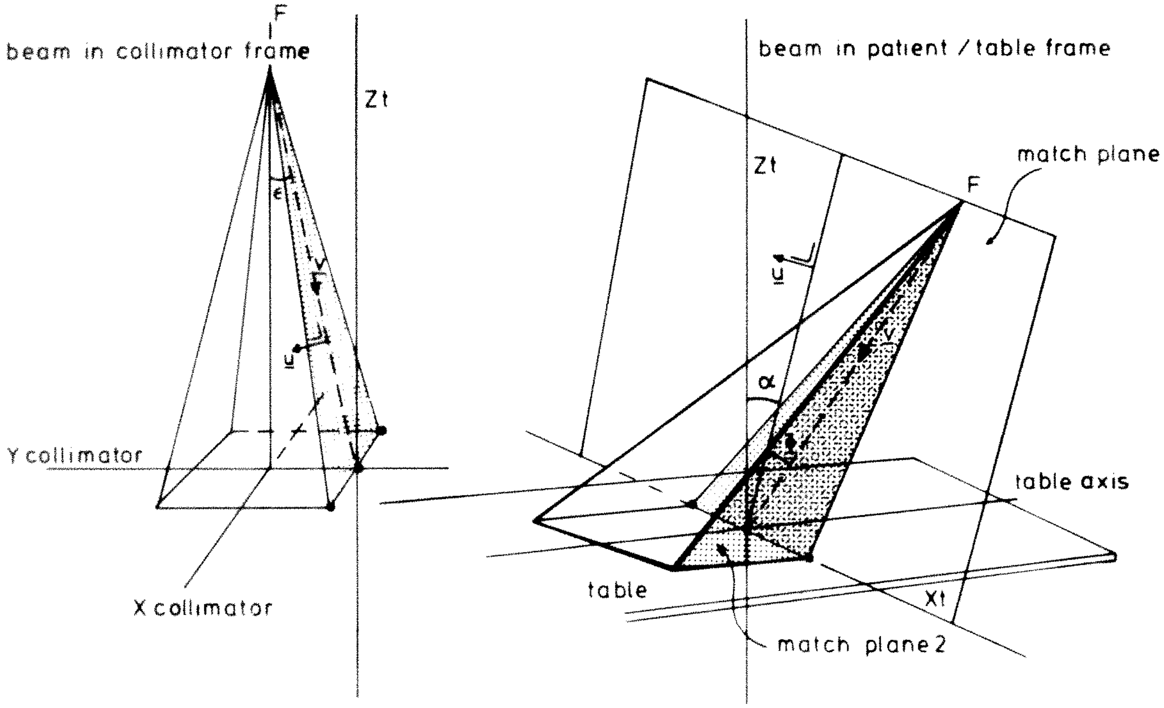

Figure 3. Beam and match plane orientation. ε is the divergence of the beam; vectors $\underline{v}$ and $\underline{u}$ define the beam orientation in the collimator frame; α is the angle between match plane 1 and the vertical in the table frame; Φ is the required orientation of the beam and thus of match plane 2.

In contrast to the half-beam technique, the angulation techniques are characterized by field deformation. Owing to the "slope" beam entrance, the field sides diverge (see insets, Fig. 2).

Two match planes

Using tangential fields in multifield breast irradiation, the opposing fields must form an opposing field match plane to diminish lung irradiation and they must form a parallel field match to the supraclavicular and axillary fields.

To match two orthogonal field sides, the asymmetrical collimator techniques produce simple straightforward matching and only one quadrant is used. The beams reduce to quarter-field techniques. As a consequence the field size is limited. However, because of the small standard wedges in most accelerators, the use of wedge techniques is further limited to very small fields. Output factors and beam profiles must be checked for every type of machine (Chui et al, 1988; Khan et al, 1986). Asymmetrical collimator techniques often have the advantage that no patient and/or equipment movements are needed between the different fields. Often the next field can be set by using collimator adjustments only. This reduces unwanted patient movement caused by table repositioning.

Using the angulation techniques described by Casebow (1984), it is not possible to match a field perfectly to two orthogonal match planes, but it is possible to match a field to one plane perfectly and match it reasonably to the other match plane, using rotations of collimators, couch and gantry. In breast irradiation, the small mismatch to the second match plane, caused by field deformation by the slope beam entrance, can be circumvented. This can be achieved by selecting as the first match plane the one between the supraclavicular and axillary fields and the tangential fields, and as the second match plane the dorsal plane of the tangential fields. The minor misalignment of this dorsal match plane is of no clinical relevance. For example, with a focus–isocentre distance of 100 cm and a field size of 10 cm × 20 cm, the angle between the field sides is 90.6°, which produces a maximum error of 0.2 cm at the field corner.

The basic set-up parameters for an isocentric treatment are the rotations of the gantry (θ_g), collimator (θ_c) and turntable (θ_t), positive if clockwise when viewed from the isocentre. The beam parameters are given in Fig. 3a, where ε is the divergence of the beam. The beam orientation in the collimator frame is characterized by the vectors $\underline{v}$ and $\underline{u}$, as indicated in Fig. 3. The angle α gives the angle between match plane 1 (the plane between the supraclavicular and axillary fields and the tangential fields) and the vertical in the table frame (Fig. 3b). The angle Φ gives the required orientation of the beam and thus of match plane 2. To make a field that has one side in match plane 2 to match plane 1, the side of the beam has to coincide with match plane 1, which is defined relative to the patient (Fig. 3b). The rotations needed to match the beam to match plane 1, if the orientation according to the patient and match plane 2 are available, are given by Casebow (1984):

$$\theta_g = \pm\cos^{-1}\cdot(\cos\Phi\cdot\cos\alpha\cdot\cos\varepsilon - \sin\alpha\cdot\sin\varepsilon) \quad (1)$$

$$\theta_c = -\sin^{-1}\cdot\frac{(\sin\varepsilon\cdot\cos\theta_g + \sin\alpha)}{\cos\varepsilon\cdot\sin\theta_g} \quad (2)$$

$$\theta_t = \sin^{-1}\cdot\frac{(\sin\alpha\cdot\cos\theta_g + \sin\varepsilon)}{\cos\varepsilon\cdot\sin\theta_g} \quad (3)$$

The formula derivations are described by Siddon (1981) and Casebow (1984) and will not be repeated here. If the match plane 1 is vertical, $\alpha = 0$.

Utrecht technique

Patient position

Using ridged foam wedges, an anti-slip mat, a variable arm support and a rubber knee support, the patient is positioned comfortably in the supine position on the treatment table with the sternum horizontal (Fig. 4). Because the use of the wedge in combination with regular arm supports limits the gantry movements, a special arm support has been developed to allow easy gantry rotation (Fig. 4). Using the two side-marks (R1, R2, Fig. 5) in combination with our laser alignment system, the patient position is defined.

Tangential fields

First the caudal and cranial borders of the selected field area are defined. The length of the fields is now defined by the distance between these borders plus 1 cm. We add 1 cm because the caudal border at the entrance of the tangential field will move cranially as a result of the field matching procedure. Typically for a 10 cm × 20 cm field the medial and lateral margins of the tangential fields will shift 1.5 cm cranially, owing to the shape of the thorax and breast; 1 cm correction is sufficient in all cases. The plane of planning is now defined as being midway between the cranial border and the caudal border plus the 1 cm. The distance between this plane and the cranial border is measured. In the plane of planning the required medial field posterior edge entrance point A is defined and its spatial co-ordinates measured (Fig. 5). If a parasternal field is used, with a flat sternum, point A will be 0.5 cm within this field to assure a reasonable matching between the parasternal and the medial tangential field. Because mostly the

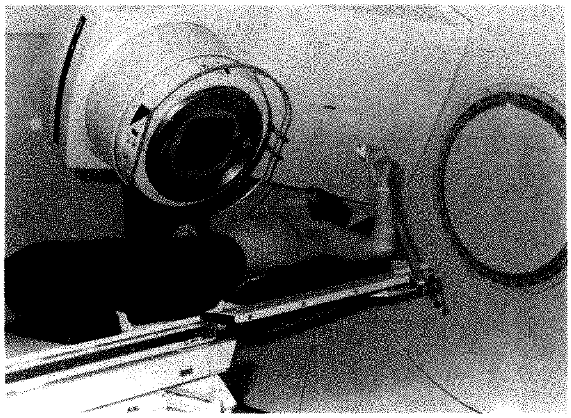

Figure 4. Example of patient position on couch. Note the horizontal sternum position, the foam table wedge and the special arm support.

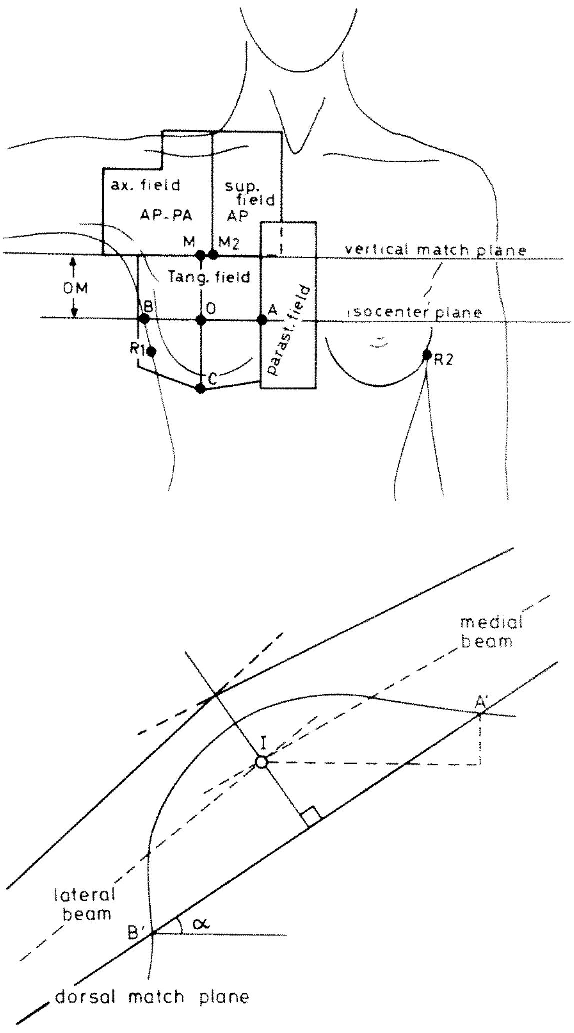

Figure 5. Diagram of field positions, see text.

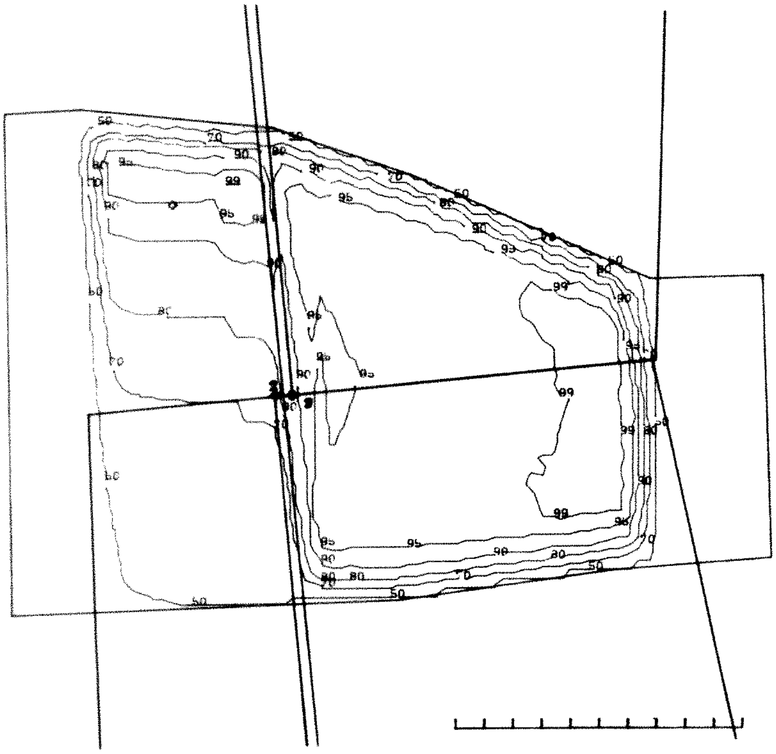

Figure 6. Typical dose distribution in the supraclavicular and axillary region. Three fields are being used: (i) a large AP field composed on the ventral axillary field and the supraclavicular area, (ii) the AP supraclavicular field, and (iii) the PA axillary field. The isodose lines shown are 85, 90, 95 and 99%.

sternum is convex, the field overlap must unfortunately be increased up to 1 cm to prevent underdosage at the field corners. This 1 cm overlap will produce a small volume with an overdosage (with a Philips SL25, 10 MV linear accelerator this volume is less than 1 cm^3 with a dose less than 120%). The overdose and thus the field overlap is energy- and machine-dependent. The lateral exit point B is defined, preferably by using the X-ray beam, and its spatial co-ordinates are measured with the laser co-ordinate system. Using the angulation technique to match the fields in the dorsal plane, the program calculates the position of the isocentre according to the fixed skin position, marker point A (Fig. 5). Using the angulation techniques of Equations 1, 2 and 3, the program then calculates the exact gantry, collimator and table rotations to make a perfect vertical cranial match plane ($\alpha = 0$) for the field matching the caudal border of the supraclavicular and axillary fields. Because the calculations are too cumbersome to do by hand they are carried out on a personal computer positioned by the simulator. The program directly accepts the simulator co-ordinates of points A and B and calculates the equipment settings according to the specific simulator co-ordinate system. Calculation during the localization procedure offers the possibility of direct simulation. During the actual irradiation, the isocentre is first defined by table movements related to the fixed point A and then the fields are positioned by the given rotation angles for the gantry, collimator and couch. The isocentre positioning according to a fixed point A is essential to guarantee an exact field matching. Isocentre positioning according to skin marks on the breast itself are too sensitive to changes in position and volume of the breast, as is often observed during a treatment course.

Using the medial tangential field radiograph of the simulator, the height of the ribs is defined and the curvature is estimated to provide the lung size information for a first-order density correction (Fraass et al, 1988). After this lung density correction, minor wedge angles are required in the tangential fields to guarantee optimal dose uniformity.

Supraclavicular field and axillary fields

A sagittal line dividing the axillary and the supraclavicular region is defined. The intersection of this line and the cranial edge of the tangential fields is called marker point M (Fig. 5). The central beam axis is defined by this point.

To cover the target area three fields are used: (i) a large antero-posterior (AP) field composed of the ventral axillary field and the supraclavicular area; (ii) the AP supraclavicular field; and (iii) the postero-anterior (PA) axillary field. All these fields are given with the central field axis through point M, which implies that asymmetrical fields are needed, both a half-beam field and two quarter-beam fields. By this isocentre orientation the vertical match plane with the tangential fields is created directly. A gantry rotation of 5° is used to avoid spinal cord irradiation. First, the large AP field is given to the required midline dose of the axillary AP–PA combination. Secondly, the field is shrunk with the lateral collimator to boost the supraclavicular field to the 3 cm depth dose. Thirdly, the gantry is rotated 180° and the PA axillary field given. Using this procedure there is an optimal lymph node dose distribution and field matching problems are prevented between the axillary fields and the supraclavicular field (Fig. 6).

A small block is applied in the axillary AP field to diminish the dose at the top of the humerus. The supraclavicular/axillary fields are given with a source–skin distance of 90 cm instead of 100 cm. The isocentre therefore lies at a depth of 10 cm below the skin surface, allowing (for our Philips simulator) enough space below the couch for the image intensifier.

Parasternal field

The parasternal field usually partly overlaps the supraclavicular field. A small block in the parasternal area overlapping the supraclavicular field is used and the centre of the parasternal field is chosen corresponding to the level of point M at the transverse dividing line between the large AP field and the tangential fields. This diminishes matching problems resulting from cranial divergence of the parasternal field. A gantry rotation of 5° is used to decrease the spinal cord dose and to improve the dose homogeneity at the match line with the medial tangential field. Depending on the location of the internal mammary lymph nodes, the ipsilateral internal mammary lymph nodes can be included in the tangential fields by the correct choice of the position of points A and B. In this case, the tangential fields include more lung tissue, but there is the benefit that there is no irradiation of the underlying lung and mediastinum from the parasternal field (Roberson et al, 1983).

Discussion

The technique presented here offers an optimal uniform dose distribution in the target areas without any overlap or gapping between the fields except for a minor area at the parasternal–medial tangential field match. This field matching was produced without any blocks and with only small couch rotations, owing to the combination of angulation techniques with asymmetrical fields. Using a special arm support the couch rotations proved to be feasible with the Philips SL25 accelerator. Because full-size tangential fields are used, we do not encounter problems with wedges that are too small to cover the half-beam alignments. Machines with wedge sizes over 40 cm can also use asymmetric fields in the tangential fields to avoid table rotations.

As discussed by Lebesque (1986), the vertical match plane in combination with the flat-sternum patient position, with the patient on a table wedge, produces so-called angled-down supraclavicular fields. We found that with an angled-down field orientation, the cranial field border of the tangential fields can be chosen to be higher, because of the geometry of the axilla. As a result this technique does not normally involve more lung than the flat patient, block techniques.

The tangential field positioning related to one fixed point A proved to be fast, practical and less sensitive to breast orientation than field positioning using central axis entrance points on the skin of the breast and marked field borders. The marked borders now serve as extra guides to verify the field settings. First-order lung correction is applied to avoid unnecessary irradiation of lung tissue. With our three-field lymph node technique, uniform doses of 50 Gy can be given safely.

The patient throughput for the actual irradiation has been improved as compared with previous techniques, while technicians judge the positional accuracy to be excellent. Patient comfort and position stability using the ridged foam wedges with the anti-slip mat proved to be sufficient.

The localization and planning descriptions and the computer program using Borland® TURBO-BASIC under MS-DOS are available free at the authors' address.

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The labelling index in carcinoma of the uterine cervix: its correlation with tumour sterilization

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Keywords: Carcinoma of the cervix, Labelling index, Cell proliferation, Tumour sterilization, Cell kinetics

Abstract. The pre-treatment labelling index (LI) was measured in 72 patients with carcinoma of the cervix. It was not correlated with patient age, stage of the disease or histological grade. 46 patients underwent hysterectomy after intracavitary irradiation with or without external radiotherapy. The mean LI in patients with tumour sterilization or microscopic residue was significantly higher than in patients with gross disease. These results suggest that tumours with low LI may be difficult to sterilize with conventional therapeutic measures, or that doomed cells may require several weeks to be eliminated in tumours with low LI.

Cell proliferation kinetics play a significant role in the prognosis of various solid tumours (Tubiana & Courdi, 1989). Only a few studies have addressed the influence of the pre-treatment percent S-phase cells in carcinoma of the uterine cervix (Dixon et al, 1977; Strang et al, 1987). These two investigations used tumour resolution and early recurrences as endpoints. Tumours of the cervix are easily accessible for biopsies. If laparotomy is conducted after irradiation, the result of radiotherapy can best be assessed by studying the pathology report of hysterectomy. It seemed interesting to attempt to match the results of surgical pathology with pre-treatment labelling index (LI).

Patients and methods

The population consisted of 72 patients with carcinoma of the cervix, treated between 1986 and 1989. The median age was 56 years, ranging between 28 and 88 years.

Grouping into stages as reported in the TNM classification (1987) yielded the following: Stage I: 24 patients (34%); Stage II: 34 patients (48%); Stage III: 10 patients (14%) and Stage IV: three patients (4%). One patient presented with vaginal recurrence. In 68 of the 72 patients (94%), the histological type was squamous cell carcinoma. Adenocarcinoma was diagnosed in three patients and adeno-acanthoma in one patient. Cell differentiation was assessed in 69 tumours. 35 (51%) were well differentiated, 28 (40%) were moderately differentiated and six (9%) were undifferentiated.

All patients had a pre-treatment evaluation of the LI. It was determined using a technique described previously (Chauvel et al, 1989). Briefly, biopsy fragments were incubated for 30 min in a culture medium containing tritiated thymidine. They were then fixed, paraffin-embedded and sectioned. Slides were dipped in Ilford K2 emulsion and exposed for 21 days at 4°C, after which they were developed, fixed and stained. Cells containing 5 grains or more were considered labelled. The LI was expressed as the number of labelled tumour cells × 100/number of total tumour cells.

Treatment consisted of two applications, each of 30 Gy, of intracavitary ^{137}Cs irradiation at a 1 month interval ($n = 38$), one application of 60 Gy ($n = 10$), or external irradiation at a dose of 45 Gy followed by one application of 20 Gy ($n = 24$). The dose-rate was 70 cGy/h at the reference isodose. Hysterectomy was carried out in 46 patients 6 weeks after intracavitary application. Most of these patients (43 of the 46) were not subjected to external irradiation before brachytherapy. Semiserial sections (1 section each 25 μ) were prepared and examined for the presence of tumour cells.

Results

The mean pre-treatment LI was 12% and the median value was 11.3% (range: 1.2–26.4%). It was not associated with the patient age (Spearman correlation coefficient $= 0.008$, $p > 0.90$). No significant differences were observed according to the stage of the disease. For Stages I to IV, the mean LI values were 12.5%, 10.8%, 12.6% and 16.0%, respectively ($p = 0.28$). Histological grading did not affect the LI either. In well differentiated tumours, the mean LI was 13%, it was 10.6% in poorly differentiated tumours and 12.5% in undifferentiated tumours ($p = 0.21$).

Upon laparotomy, examination of the operative specimen demonstrated that 21 out of 46 patients had tumour sterilization, 17 and 8 patients had microscopic and macroscopic tumour residue, respectively. The mean pre-treatment LI in those with macroscopic tumour residue was 7.6%, *versus* 12.2% in the other

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Table I. LI in different patient categories

	n	LI (%)	
All patients	72	12	
Stage			
I	24	12.5	
II	34	10.8	not significant
III	10	12.6	
IV	3	16	
Grading			
well differentiated	35	13	
poorly differentiated	28	10.6	not significant
undifferentiated	6	12.5	
Operative specimen			
sterilization	21	12.2	
microscopic residue	17		$p = 0.02$
gross disease	8	7.6	

patients ($p = 0.02$). These results are summarized in Table I.

Discussion

The median LI value is identical to that reported by us and others in squamous cell carcinoma of the head and neck (Silvestrini et al, 1984; Chauvel et al, 1989), and slightly higher than that reported by Dixon et al (1977) for cervical carcinoma (mean value: 7.8%). It was not correlated with the patient age, stage or tumour differentiation.

In patients subjected to hysterectomy, the presence of gross disease was associated with a low initial LI, which is an unexpected result.

With regard to cell kinetics and radiosensitivity of solid tumours, short term tumour response should be dissociated from long term outcome. Although it has been observed that histological groups of human tumours with high LI are more radioresponsive (Malaise et al, 1978), this does not mean that they are more radiocurable. In carcinoma of the uterine cervix, Dixon et al (1977) noticed that the mean LI was higher in radioresponsive tumours, though not reaching statistical significance. Furthermore, the higher the mean LI, the earlier the tumour resolved. In other studies, no relationship could be found between the pre-treatment LI and the short term response, assessed clinically, in various solid tumours (Elequin et al, 1978; Courdi et al, 1980; Silvestrini et al, 1984). However, cell depletion after radiotherapy was more important in tumours with high pre-treatment LI (Courdi et al, 1980). A comparable result was reported by Silvestrini et al (1984), who noticed that most fast proliferating tumours demonstrated a marked inhibition of proliferative activity after 10 Gy. We have looked for a possible influence of the pre-treatment LI on the clinical findings upon the second intracavitary application. The mean LI in cases with complete response was 11.8%. It was 11.7% in patients with good tumour reponse and 10.2% in cases with either poor or no response (not significant).

Concerning the long term patient outcome, it is admitted widely that cell proliferation kinetics are of high prognostic significance in several types of cancer. A recent survey showed clearly that tumours with high S-phase fraction have a poor prognosis in terms of survival or relapse-free survival and this factor is often independent (Tubiana & Courdi, 1989).

In the present study the LI was matched with the histological findings following laparotomy. There are several possible interpretations of these results. Although the presence of tumour as stated in the pathology report means the identification of viable tumour cells, it is not excluded that these cells may be doomed to die, in spite of the relatively long delay between the intracavitary application and surgery (6 weeks). Doomed cells may require a long time to be eliminated in tumours with low LI, thus explaining the association between low LI and the presence of gross pelvic disease. Another possibility is that tumours with low LI are more difficult to sterilize due to either an inherent radioresistance, which is most unlikely, or an association with an unfavourable condition, such as hypoxia. Although possible, this last interpretation would contradict the good prognosis of low LI tumours in general. Finally, these results may be a chance finding, especially as the number of patients is low and the treatment not uniform. Extending the follow-up of these patients would tell us how these findings would be related with the long term outcome.

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Biological intercomparisons of neutron beams used for radiotherapy generated by $p^+ \rightarrow Be$ in hospital-based cyclotrons

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Keywords: Neutron therapy, Biological intercomparisons, Relative biological effectiveness

Abstract. The new generation of hospital-based neutron therapy facilities involve cyclotrons using protons on beryllium. The spectrum of neutrons produced includes a large and variable proportion of low-energy neutrons that are poorly penetrating but biologically effective. Cells cultured *in vitro* were used to compare the three US facilities at Seattle, M.D. Anderson and UCLA, together with the UK facility at Clatterbridge. Cyclotrons were compared within a given experiment on the same day using cells from a common suspension. Among the three US facilities, the relative potency factor at a depth of 25 mm differs by about 11%, with Seattle the least and UCLA the most biologically effective. Clatterbridge was compared directly with M.D. Anderson and found to be less effective by about 5%; it has a slightly lower biological effectiveness than any of the US facilities. There is evidence for an increased biological effectiveness in the build-up region, which reduces the effective skin sparing potential. There is not much difference in build-up between the three US facilities. Using the proton-on-beryllium neutron production process results in a wide spectrum of neutrons with a large but variable low-energy component. The biological effectiveness of the beam depends on target design and thickness as well as the design of the collimating system. Consequently the biological effectiveness of neutron beams generated by this process must be assessed on an individual basis. It cannot be assumed that because cyclotrons have similar accelerating energies that the relative biological effectiveness will be the same.

Stone and his colleagues at Berkeley were the first to use neutrons for radiotherapy in the late 1930s; this early study resulted in unacceptable late sequelae and was terminated abruptly by the entry of the United States (US) into World War II (Stone, 1948; Sheline et al, 1971). Interest in the use of neutrons for the treatment of human cancer was rekindled in the late 1950s at the Hammersmith Hospital in London, where patient treatment was not started until an impressive amount of careful experimentation had been completed in both radiological physics and radiation biology. This well documented work formed the basis for the first clinical trials (Fowler et al, 1963; Bewley, 1963; Catterall, 1974, 1977). The early success of the Hammersmith group inspired interest on both sides of the Atlantic as well as in Japan in the possibility of establishing additional clinical neutron facilities (Griffin et al, 1979; Tsunemoto et al, 1979).

In the US, these took the form of large cyclotrons, initially built for high-energy physics research and therefore often located in physics departments remote from major hospitals and having a fixed horizontal or vertical beam (Griffin et al, 1979). Under these circumstances it proved difficult to treat effectively a large number of patients in randomized clinical trials. The new generation of neutron therapy machines, therefore, in both the US and Great Britain are hospital-based cyclotrons, having good depth–dose characteristics, a high output and an isocentric mount. A more compact machine that can be accommodated in a hospital is made possible by changing the neutron production process from deuterons on beryllium to protons on beryllium (Bonnett et al, 1988). A cyclotron accelerating protons to a given energy is, of course, much smaller and more compact than one accelerating deuterons. However, other complications arise from the change of the accelerated particle. In the case of $d^+ \rightarrow Be$, the neutrons produced have a spectrum with a single peak, while the $p^+ \rightarrow Be$ process results in a neutron beam with a large component of both low-energy and high-energy neutrons. The beams are, therefore, very different. Some, though not all, of the beams in clinical use have been characterized spectroscopically using time of flight measurements (e.g. Crout et al, 1991). However, one problem with this technique is that it is limited to energies above ~ 2 MeV, thus the low-energy component is rarely known.

Intercomparisons

Because of the substantial cost and investment of effort involved in the implementation of neutron clinical trials, the value of full co-operation between the few centres using these particles has been recognized from the outset.

A great deal of effort was expended by the physicists at the various installations used for neutron therapy to achieve compatible dosimetry, and intercomparisons indicate agreement in the measurement of physical dose to within a few per cent (Smith et al, 1975; Broerse et al, 1981). However, compatible dosimetry does not of itself allow the radiotherapist to compare dosage schedules directly, since the varying neutron energies result in a different relative biological effectiveness (RBE) for each neutron beam.

In order to facilitate the pooling of experience and a comparison of clinical results, a number of individuals have undertaken biological intercomparisons using portable model systems (Hall et al, 1975, 1979; Todd et al, 1975; Hall, 1977; Hall & Kellerer, 1979).

Previous intercomparisons of the earlier generation of neutron facilities, which mostly employed the $d^+ \rightarrow$ Be production process, showed RBE to be a function largely of the energy of the accelerated deuteron. Based on experiments performed in the US, Great Britain and Japan, RBE values plotted as a function of deuteron energy fell around a common line with RBE decreasing with increasing energy (Hall & Kellerer, 1979; Hall et al, 1979). The same cannot be said for the new generation of hospital-based cyclotrons where neutrons are generated by the $p^+ \rightarrow$ Be reaction; RBE values from different facilities do not show a simple relationship to proton energy. It is true that RBE varies linearly with proton energy if experiments are performed on a single machine in which the energy is varied (Beauduin et al, 1989), but it is no longer true when the range of energies involves different facilities. The obvious conclusion from this observation is that factors other than proton energy are of more importance—these include target design and collimator configuration (Hall et al, 1982; Hall et al, 1983; Hornsey et al, 1988; Bewley et al, 1989).

The present paper describes biological comparisons between three hospital-based neutron facilities in the US and one in Great Britain. The characteristics of the machines are listed in Table I.

Materials and methods

Chinese hamster V79 cells cultured *in vitro* were used in this series of comparison experiments. Cells were grown using standard tissue-culture techniques in Ham's F10 supplemented with 10% fetal bovine serum (Sterile Systems), antibiotics (Gibco), and L-Glutamine (Gibco).

In order to exploit fully the precision of which the *in vitro* system is capable, attached cells were used and cyclotrons were compared within a given experiment on the same day. For cells in culture, variations within an experiment are much smaller than between experiments. Within a given experiment, the repeatability between replicate flasks is limited only by the counting statistics, and since large numbers of colonies can be used, the accuracy is of the order of a few per cent.

By contrast, when experiments are repeated on separate occasions, it is not unusual for the cell surviving fraction at a given dose level to differ by a factor of 2. For this reason, the system was adopted of comparing facilities within a given experiment. The details have been published previously (Hall et al, 1982, 1983). For each experiment, exponentially growing V79 cells were harvested, spun down and counted, and plated into 25-cm^2 (Corning) tissue-culture flasks. The cells were allowed to attach overnight. On the morning of the experiment, the flasks were completely filled with ice-cold medium (to stop the cells from cycling) and placed into specially constructed, temperature-controlled carriers for transport to the respective cyclotrons.

The carriers consist of standard pressure cookers sealed to avoid changes of pressure when aircraft take-off and land. The pressure cooker is surrounded by insulation and frozen material. The intent is to maintain the temperature within the range 10–18°C. It was found by trial and error that a temperature in this range preserved plating efficiency at 80–90% and prevented cells from moving through the cell cycle. If the temperature is allowed to exceed 22°C, cells begin to move through the cycle. One set of flasks was flown to each of the facilities to be compared.

Experiment I

In this experiment the three US facilities were compared, namely UCLA, Seattle and M. D. Anderson. The question that prompted the experiment was the clinical observation that skin reactions appeared to be more severe at some facilities than others. Flasks were irradiated simultaneously at the three facilities using the lucite phantom illustrated in Fig. 1. Cells were irradiated at depths of 1 mm (the thickness of the tissue culture flask) and at 25 mm. The doses were prescribed at a depth of 25 mm, which is close to the build-up depth, based on measurements with an ionization chamber in the phantom.

Table I. Characteristics of the four neutron facilities studied

Location	Manufacturer	Energy of accelerated proton (MeV)
UCLA, Los Angeles, US	Cyclotron Corporation	45
M.D. Anderson Hospital, Houston, US	Cyclotron Corporation	42
University of Washington, Seattle, US	Scanditronix	50
Clatterbridge, UK	Scanditronix	62

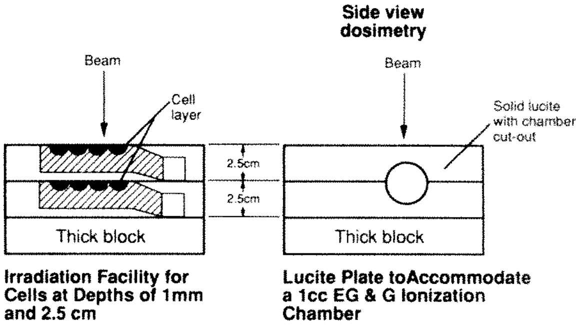

Figure 1. Set-up for irradiation of monolayers of cells at depths of 1 mm and 25 mm at the three US neutron facilities.

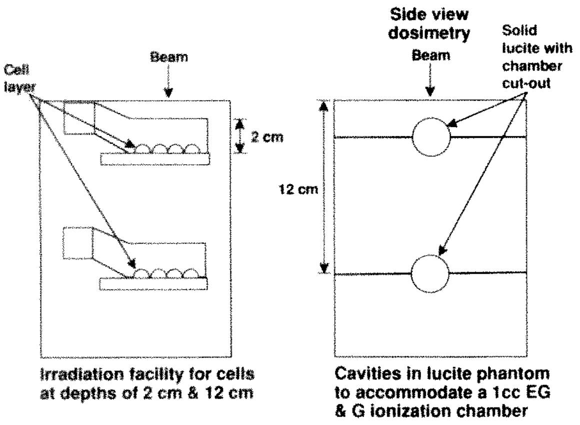
Cell layer
Beam
2 cm
12 cm
Side view dosimetry
Beam
Solid lucite with chamber cut-out
Irradiation facility for cells at depths of 2 cm & 12 cm
Cavities in lucite phantom to accommodate a 1cc EG & G ionization chamber

Figure 2. Set-up for irradiation of monolayers of cells at depths of 20 and 120 mm at neutron facilities in the US and United Kingdom.

Experiment II

In this experiment, the UK facility at Clatterbridge was compared with M.D. Anderson. This experiment addressed a somewhat different question, namely the possibility of a changing neutron RBE with depth. Flasks were irradiated at depths of 20 and 120 mm using the lucite phantom illustrated in Fig. 2. Irradiations were performed at Clatterbridge with and without the addition of a hydrogenous filter. The M. D. Anderson beam is always filtered.

Following irradiation in either experiment, the flasks were returned to the carriers, transported back to Columbia and placed in an incubator. The exception was Clatterbridge, where the cells were incubated on site. Cells were incubated for a period of 6 days to allow for colony formation, after which the clones were fixed and stained with formalin and giemsa, and scored. A colony was scored as a surviving cell if it contained 50 or more cells.

The survival data were analysed using curves of the same shape, with a dose modifying factor which was varied from beam to beam to fit the data. A single dose factor is then a measure of the RBE or relative potency, between the beams, based on the data accumulated over the entire dose range. It is only a meaningful concept when comparing two neutron beams that are close in energy. When comparing, for example, neutrons with X-rays, RBE clearly varies with dose. To be specific our technique for comparing one set of survival data with another (or others) involves fitting the survival data to the expressions

$$S_i(D) = \exp(-\alpha f_i D - \beta f_i^2 D^2)$$

where the subscript i refers to different irradiation protocols (e.g. different depths or different machines). Thus f_i is an estimator of the dose modifying effect, of one radiation relative to another. It is sometimes referred to as the "relative potency" (Hall et al, 1982). The estimation of the parameters [α, β, f_i] was achieved using the maximum likelihood technique described elsewhere (Brenner & Hall, 1991).

Results

Experiment I

The survival curves for cells irradiated at a depth of 25 mm at UCLA, Seattle and M. D. Anderson are shown in Fig. 3a. The relative potency factors between the three facilities at a depth of 25 mm, calculated as described above, are shown in Table II. It is clear from Table II and Fig. 3a that the UCLA machine is biologi-

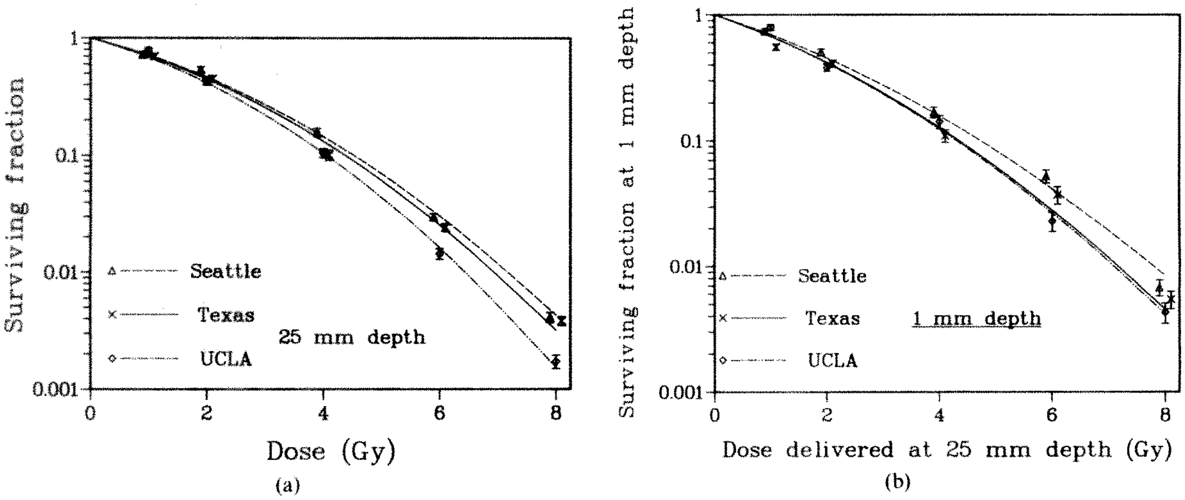

Figure 3. (a) Survival data for V79 Chinese hamster cells exposed to graded doses of neutrons at a depth of 25 mm at the three US neutron facilities. In this and subsequent figures the curves are fits to the linear-quadratic equation as described in the text. In addition, in all figures the error bars are standard errors determined by binomial statistics. (b) Survival data for V79 Chinese hamster cells exposed at a depth of 1 mm at the three US neutron facilities. Doses were prescribed at a depth of 25 mm and are thus roughly 25–30% larger than those delivered at 1 mm (see text).

Table II. Relative potency factors for the three US facilities at a depth of 25 mm

Seattle	1.0
M.D. Anderson	1.030±0.047
UCLA	1.115±0.039

Table III. Biological build-up factors, i.e. ratio of biologically effective doses relative at 1 mm to 25 mm (see text)

M.D. Anderson	0.94±0.03
Seattle	0.97±0.03
UCLA	0.92±0.04

cally more effective per unit dose than the two other US facilities.

The survival curves for cells irradiated at a depth of 1 mm at the three facilities are shown in Fig. 3b; the doses shown are those prescribed at a depth of 25 mm. Table III shows the biological build-up factors for the three facilities, i.e. the ratio of biologically effective doses at 1 mm to 25 mm. These ratios are, in effect, the product of two factors, namely the dose build-up factor and the relative potencies of the radiation between the depths of 1 and 25 mm. The physical dose build-up factor from 1 mm for a large field of 42 or 66 MeV $p^+ \rightarrow Be$ neutrons has been reported to be in the range 0.75–0.8 (Mijnheer et al, 1978; Awschalom & Rosenberg, 1981; Horton et al, 1988). Since, the biological build-up factors are in the range from 0.92 to 0.96, this implies a relative potency of perhaps 1.2–1.3 at 1 mm compared with 25 mm. Such an increase probably reflects the soft neutron component of the beam, and will vary strongly with individual irradiation conditions.

Experiment II

Cell survival curves for cells irradiated at a depth of 20 mm at M.D. Anderson and Clatterbridge are shown in Figs 4 and 5. In both cases the M. D. Anderson beam was filtered by a hydrogenous filter; all data in Fig. 4 relate to a filtered beam at Clatterbridge, while the data in Fig. 5 relate to an unfiltered beam at Clatterbridge. Figure 6 contains data from Clatterbridge for irradiations at depths of 20 and 120 mm. Relative potency factors from the data shown in Figs 4, 5 and 6 are summarized in Table IV. There are several conclusions to be drawn. First, the M. D. Anderson beam is biologically more effective than the Clatterbridge beam by about 4–7%. Second, the addition of a hydrogenous filter makes little difference to the Clatterbridge beam, nor does RBE vary much with depth. This confirms earlier reports concerning Clatterbridge, but is quite different to the situation at other facilities using the $p^+ \rightarrow Be$ reaction (Bewley et al, 1989; Hall et al, 1982, 1983).

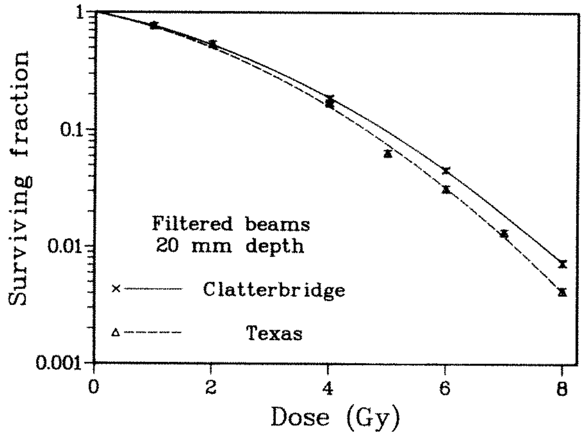

Figure 4. Survival data for V79 Chinese hamster cells irradiated with graded doses of neutrons at a depth of 20 mm with filtered beams at Clatterbridge and M. D. Anderson Hospital, Houston.

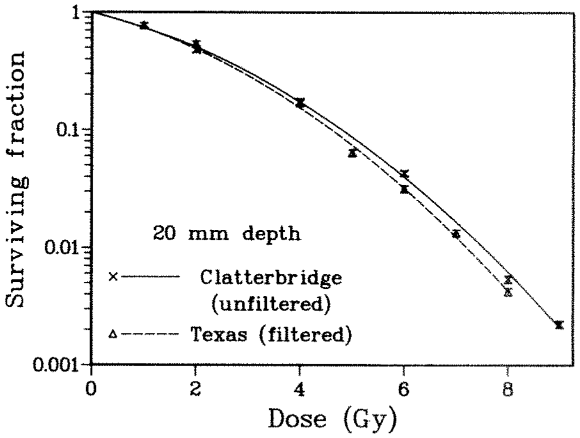

Figure 5. Survival data for V79 Chinese hamster cells irradiated with graded doses of neutrons at a depth of 20 mm with an unfiltered beam at Clatterbridge and a filtered beam at M. D. Anderson Hospital, Houston, Texas.

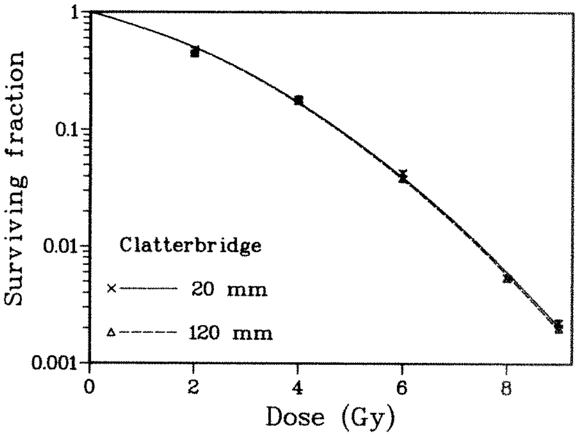

Figure 6. Survival data for V79 Chinese hamster cells irradiated with graded doses of neutrons at depths of 20 and 120 mm at Clatterbridge, UK.

Table IV. Relative potency factors for the Clatterbridge and M.D. Anderson neutron therapy facilities

	20 mm depth
Clatterbridge (filtered)	1.0
Clatterbridge unfiltered	1.029 ± 0.038
Clatterbridge filtered	1.0
M.D. Anderson filtered	1.069 ± 0.033
Clatterbridge unfiltered	1.0
M.D. Anderson filtered	1.044 ± 0.026
Clatterbridge	20 mm: 1.0
Clatterbridge	120 mm: 1.007 ± 0.019

Discussion

The general conclusion that can be drawn from the data in this paper, together with previous experience, is that RBE values of cyclotron-produced neutron beams using the $p^+ \rightarrow Be$ reaction need to be assessed on an individual basis. It cannot be assumed that because different cyclotrons have the same accelerating energy, the RBE will be the same. Nor can it it be assumed that RBE will necessarily decrease with increasing energy of the accelerated proton. It further follows that if a common protocol is used at several facilities under the auspices of a co-operative group, it is not necessarily appropriate to use a common dose level, however carefully the physical dosimetry is compared.

It has previously been reported that for high-energy neutron beams generated by $p^+ \rightarrow Be$, there may be a change of RBE with depth, which can be reduced or eliminated by the use of a hydrogenous filter, and that this change of RBE is highly variable between different facilities (Hall et al, 1983; Hornsey et al, 1988). The data in the present paper may be briefly summarized as follows: amongst the three US neutron facilities, relative potencies at a depth of 25 mm differ by about 11% with Seattle the least biologically effective and UCLA the most effective. Clatterbridge is less effective than M. D. Anderson by about 5% and is therefore slightly less effective than any of the US machines. In terms of the biological build-up between 1 mm and 25 mm, i.e. the ratio of biological effective doses between these depths, there is a small variation between the three US machines with UCLA showing the largest difference between depths and M. D. Anderson the smallest. Based on an assumed dose build-up factor of 0.75–0.8, the relative potency for the neutrons at 1 mm is probably about 1.2–1.3 compared with at 25 mm (Table III).

The changing RBE with depth and the finding in the present paper that RBE is not a simple function of proton energy are both manifestations of the shape of the neutron spectum generated by the $p^+ \rightarrow Be$ process. A wide spectrum of neutrons is produced including a substantial (but variable) low-energy component, which is highly effective biologically and is filtered out preferentially in the first few centimetres of absorbing material. The RBE of the neutron beam, particularly at shallow depths, is critically dependent on target thickness and design, as well as the design of the collimating system, all factors that have major influence on the magnitude of the low-energy neutron component of the beam. As discussed above, this low-energy component is rarely measured, as it is not accessible by time-of-flight techniques. It is, however, measurable using activation techniques, as demonstrated by Greenwood et al (1979) for a 60 MeV $d^+ \rightarrow Be$ beam.

Spectral measurements and the determination of microdosimetric quantities in a few of the high-energy beams confirm the explanation that the RBE fluctuations are a consequence of a variable low-energy neutron component, but insufficient physical measurements have been performed (certainly at the US facilities) to allow a detailed correlation to be made between physical and biological parameters.

Acknowledgments

Intercomparison experiments of this kind are only possible with the unstinting help and co-operation of colleagues at all of the institutions involved. These include: Drs David Bewley, John Parnall and David Bonnett at Clatterbridge; Drs Robert Parker, James Smathers and Ms Kathy Mason at UCLA; Drs Lester Peters, John Horton and Pat Stafford at M. D. Anderson Hospital, Houston, Texas; Drs Tom Griffin, Juri Eenmaa and Peter Wootton at the University of Washington, Seattle. This investigation was supported by Grant Numbers CA 12536 and CA 18506 from the National Cancer Institute.

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Technical note

What to do with the biopsy specimen — practice in an oncology setting

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The technique of image-guided biopsy using either fluoroscopy, ultrasound or computerized tomography (CT) has become well established in recent years. It is now routine practice in most radiology departments having been shown to have an accuracy of greater than 90–95% (Gazelle & Haaga, 1989; Jennings et al, 1989; Charboneau et al, 1990) and using biopsy needles of 18 gauge or smaller, has a complication rate of less than 1% in many series (Welch et al, 1989; Nolsoe et al, 1990). It makes an important impact on clinical management (Jaeger et al, 1990), allowing diagnosis and treatment planning without recourse to more invasive methods. The automated spring-loaded biopsy gun has simplified the procedure (Parker et al, 1989; Bernardino, 1990) producing adequate specimens without crush artefact and with minimal trauma to the patient.

While most series have concentrated on the technique of image-guided biopsy, little emphasis has been placed on the importance of optimal preparation of tissue specimens once obtained. At the Royal Marsden Hospital, London, we perform over 100 CT-guided biopsies annually for a wide range of primary and secondary malignancies, together with other occasional incidental or complicating pathologies. As a referral centre, this includes difficult cases where previous biopsy results may have shown malignancy but of indeterminate type. Given the likely diagnosis based on clinical and radiological findings, close liaison with the histopathologist with regard to the type of tissue preservative is of the utmost importance in maximizing the diagnostic yield from specimens obtained. Once preserved, careful transport and manipulation of biopsy core specimens is essential to avoid fragmentation. We follow a simple protocol for preserving our tissue specimens before they reach the pathology laboratory (Table I).

Based on the clinical presentation and radiological findings, the diagnosis of tumour type can often be made with a moderate degree of confidence. Once alerted to the probable diagnosis, the strategy to obtain biopsy confirmation should not only include planning the guiding imaging modality and the route of the biopsy track, but also the type of preservative in which the specimen should be placed. This will ensure the best chance of a complete diagnosis from a single attendance for percutaneous guided biopsy.

The radiologist or clinician having obtained a satisfactory biopsy specimen has three alternatives. Preserving the specimen in 10% formol-saline fixative is universal, if not the sole practice in most departments. This will suffice in the majority of cases and allow a histological diagnosis to be made using light microscopy with or without immunohistochemical examination of formalin-fixed paraffin-embedded tissue. However, there are specific situations where further tissue preparation may be helpful.

Whilst electron microscopy can be performed on formalin-fixed tissue, optimal preservation can be obtained by placing a portion of the tissue specimen in glutaraldehyde, available in small bottles as 4% glutaraldehyde in 0.125 M phosphate buffer. Electron microscopy is particularly useful in the diagnosis of soft tissue

Table I. A suggested scheme for preparation of biopsy specimens

Suspected diagnosis	Preferred preparation/preservative
Lymphoma	Formalin for light microscopy Fresh specimen for chromosomal studies for subtyping and occasionally for frozen material
Sarcoma	Formalin for light microscopy Glutaraldehyde for electron microscopy
Breast carcinoma	Formalin for light microscopy Fresh specimen to freeze for oestrogen receptor studies
Melanoma	Formalin for light microscopy Glutaraldehyde for electron microscopy occasionally useful
Mesothelioma	Formalin for light microscopy Glutaraldehyde for electron microscopy occasionally
Carcinoma	Formalin for light microscopy
Other	Formalin for light microscopy Discussion with pathologist in unusual or difficult cases

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sarcoma (Fisher, 1990) and occasionally of value in diagnosing melanoma and mesothelioma (Warhol & Corson, 1985). In patients who previously have posed diagnostic problems on light microscopy, particularly with anaplastic polygonal cell tumours and with spindle cell tumours, electron microscopy in conjunction with immunohistochemistry can be of value in advancing the differential diagnosis (Fisher et al, 1985).

Fresh tissue should be obtained in cases of suspected lymphoma to allow chromosomal analysis for subtyping and in breast carcinoma for oestrogen receptor studies. In doubtful cases, fresh specimens in addition to formalin-fixed tissue should be obtained to allow appropriate tissue processing, tailored to the range of possible differential diagnoses.

Before biopsy with an 18 gauge needle, we often perform fine needle (20 or 21 gauge) aspiration for cytology. This is particularly helpful in cases where a diagnosis of malignancy only is required, for instance, in the confirmation of metastatic involvement in the patient with a known primary and in the diagnosis of the type of carcinoma. Often the tumour type can be determined on cytology alone. However, whilst there are occasions where cytology or fragment analysis has been positive when histology has not, it is generally accepted that histological examination of a solid core specimen produces more information (Rode, 1989). The use of an 18 gauge needle fired by the biopsy gun produces diagnostically adequate specimens with a very low complication rate and, unless there is a specific contra-indication, it is our practice to follow the initial fine needle aspiration with biopsy.

With advances in imaging techniques and with the advent of spring-loaded biopsy devices enabling diagnostically sufficient core specimens to be obtained with small biopsy needles, the radiologist is in a privileged position to obtain tissue safely from virtually any target organ in the body.

The radiologist performing the biopsy will have made a short list of differential diagnoses, if not the most likely diagnosis, based on the radiological appearances. Being aware of the different histopathological requirements in specific situations, he will be able to tailor the biopsy procedure, according to the number of specimens and their preservation requirements, in order to maximize the diagnostic yield.

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Case reports

CT of a unicameral bone cyst in a rib

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Unicameral bone cysts are relatively common lesions in childhood but are distinctly unusual in the ribs; a single case having been reported previously (Shulman et al, 1977). They occur most frequently in the metaphysis of the proximal ends of the humerus or femur (Jaffe et al, 1942; Baker, 1970). There is an age dependency of the location of these lesions, the most common site after the age of 17 years being the pelvis and os calcis (Norman & Schiffman, 1977). The lesion shows a male predominance.

The computed tomographic (CT) appearance of unicameral bone cysts has been described infrequently. These lesions have a low attenuation value (0–20 Hounsfield Units (HU)) (Blumberg, 1981). We report on the CT appearance of a unicameral bone cyst of the rib. This also had a low attenuation (18 HU). The low attenuation and the homogeneous appearance may be characteristic enough for this lesion to allow pre-operative diagnosis.

Case report

An athletic, 17-year-old male had previously noticed a tender swelling over the right lateral mid-chest. While playing sports, he noted a sudden onset of right chest pain, made worse on deep inspiration. The postero-anterior chest radiograph demonstrated an expansile lesion involving the right sixth rib. The margins appeared somewhat sclerotic and without periosteal reaction, but no other diagnostic features could be discerned.

A CT scan was performed with intravenous administration of contrast. This examination showed the lesion to have a homogeneous appearance with an attenuation value of 18 HU. The cortex appeared sclerotic but thinned and a lucent line was present through the lateral cortex on a single slice, presumably representing a pathologic fracture (Fig. 1). No extraosseous soft tissue component was present.

At the time of open biopsy the lesion was found to be cystic and containing clear yellow fluid. The cyst wall was composed of finely vascular fibrous tissue. Haemosiderin was present but not conspicuous and new osteoid was present only focally in the cortex overlying the lesion. No callus was found, giant cells were sparse and there was no evidence of an underlying neoplasm.

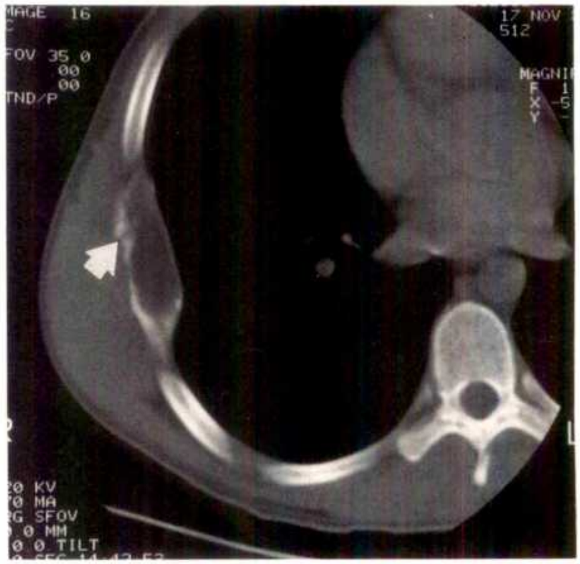

Figure 1. Transverse scan through unicameral bone cyst of right sixth rib on bone settings. Note expansile lesion with sclerotic but thinned cortex. The lucent line (arrow) on the lateral aspect of the lesion presumably represents a pathological fracture. No soft tissue mass was present (adjacent soft tissue represents muscle and was present contralaterally).

Discussion

While unicameral (solitary) bone cyst is a relatively common entity in the long bones, the pelvis or the calcaneus location in a rib is extremely unusual. A case review of 45 unicameral bone cysts by Baker (1970) demonstrated no rib lesions. Of 1402 primary bone tumours and tumour-like lesions reviewed in another series, 52 occurred in the ribs and only one of these was a solitary cyst (Netherlands Committee on Bone Tumours, 1966). A review of the English and German literature by Gayler and Donner (1967) reported 159 benign rib lesions in adults, none of which were solitary bone cysts.

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Unicameral cysts tend to be more aggressive in childhood, with the highest incidence of pathologic fractures under 10 years of age. The presence of a lucent line through the lateral aspect of this lesion was felt to represent a pathologic fracture, as unicameral cysts themselves do not breach the cortex without an associated fracture. The fracture site was not found pathologically in this case, although this was presumably caused by sampling error since the lesion was curetted rather than excised.

In this case, before CT, the differential diagnosis included fibrous dysplasia, aneurysmal bone cysts (ABC), giant cell tumour, enchondroma and Ewing's sarcoma. The CT examination was helpful in characterizing the lesion, although open biopsy was necessary for definitive diagnosis. The low attenuation value of the central component was suggestive of a fluid matrix. Fibrous dysplasia would be expected to contain fibrous or solid tissue of higher density with attenuation values of greater than 70 HU (Blumberg, 1981).

Aneurysmal bone cyst may demonstrate an inhomogeneous matrix, often with bony trabeculations and attenuation values of 20–78 HU pre-contrast and 23–157 HU post-contrast administration (Hudson et al, 1984). CT has been used to demonstrate fluid levels within ABCs (Hudson, 1984).

In giant cell tumour of bone attenuation, values are usually of 25–72 HU pre-contrast (mean = 44 HU) and 36–132 HU (mean = 63 HU) post-contrast administration. However, lesions of lower attentuation may occur, with pre-contrast attenuation values of 8–14 HU and post-contrast values of 15–21 HU (Hudson et al, 1984). These low attenuation values have not been described in giant cell tumour of the ribs. Some giant cell tumours may not demonstrate significant contrast enhancement (De Santos & Murray, 1978).

We conclude that the finding of a homogeneous cystic bone lesion on CT with an attenuation of less than 20 HU is highly suggestive of simple bone cyst.

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Malignant paraganglioma of the mediastinum: a further diagnostic and therapeutic use of radiolabelled mIBG

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Keywords: Paraganglioma, mIBG

The paraganglia are widely dispersed collections of specialized neural crest cells arising in association with the segmental or collateral autonomic ganglia (Enzinger & Weiss, 1988). The extra-adrenal paraganglia can be best classified by their anatomical site (Glenner & Grimley, 1974).

(1) Branchiomeric paraganglia arise in association with

the arteries and cranial nerves of the head and neck. Carotid body and glomus jugulare tumours are neoplasms arising from these paraganglia.

(2) Intravagal paraganglia are located within the perineurium of the vagus nerve and a vagus body tumour is an example of this type.

(3) Aorticosympathetic paraganglia arise in association with the sympathetic nervous system. Aortic body tumours and retroperitoneal paragangliomas are examples of tumours from these paraganglia.

Paragangliomas are further classified as to whether functional activity is present. Carotid body and aortic body tumours are usually non-functional whereas some sympathetic paragangliomas may be virtually indistinguishable from adrenal phaeochromocytomas. In the mediastinum, paragangliomas known as aortic body tumours arise from the chemoreceptor paraganglia associated with the pulmonary artery or aortic arch. Alternatively they may arise from the sympathetic chain and so are similar to the extra-adrenal retroperitoneal paragangliomas. Mediastinal paragangliomas arising from the paraganglia associated with the sympathetic chain are far less common than aortic body tumours (Enzinger & Weiss, 1988). A recent review of the literature cited that only seven of 47 reported cases of mediastinal paragangliomas arising from the sympathetic chain exhibited metastases, and of these seven only two had elevated serum and urinary catecholamines (Odze & Begin, 1990).

Metaiodobenzylguanidine (mIBG) is an analogue of the adrenergic neurone blocker guanethidine. It possesses specific affinity for adrenergic neurones and the adrenal medulla and in its ^{123}I-labelled form has been used for the scintigraphic localization of phaechromocytomas, paragangliomas and other neural crest tumours (Moll et al, 1987). Uptake of radiolabelled mIBG does not correlate with the catecholamine secretory activity of the tumour (Khafagi et al, 1987). In the form of ^{131}I-mIBG it has been used as a therapeutic agent in neuroblastoma and other neuroendocrine tumours, including carcinoid and medullary carcinoma of the thyroid (Sandler, 1988). Previously reported cases of metastasizing mediastinal paragangliomas arising from the sympathetic chain have been treated with a combination of resection, radiotherapy and chemotherapy but not with radiopharmaceuticals (Odze & Begin, 1990). ^{131}I-mIBG has been used to treat bone metastases in metastasizing, non-functioning retroperitoneal paragangliomas (Baulieu et al, 1988).

Case Report

A 36-year-old male ex-smoker presented in February 1987 with a right Horners syndrome and right superior mediastinal mass. The mass was excised. This was thought to be a Pancoast tumour and a total excision of the mass was attempted. At operation the mass appeared to arise from the sympathetic trunk. A pathological diagnosis of malignant epithelial tumour was made, probably a metastasis. A bone scan in February 1988, which was performed because the patient had developed chest wall pain, showed further deposits in the left 3rd rib and

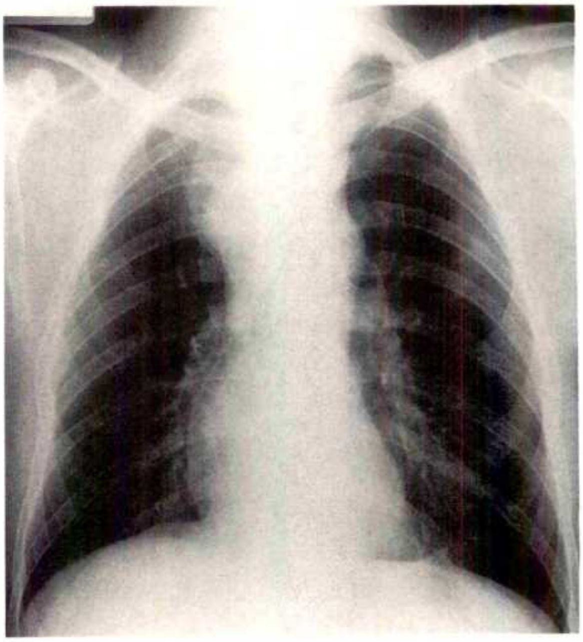

Figure 1. Chest radiograph showing right superior mediastinal mass.

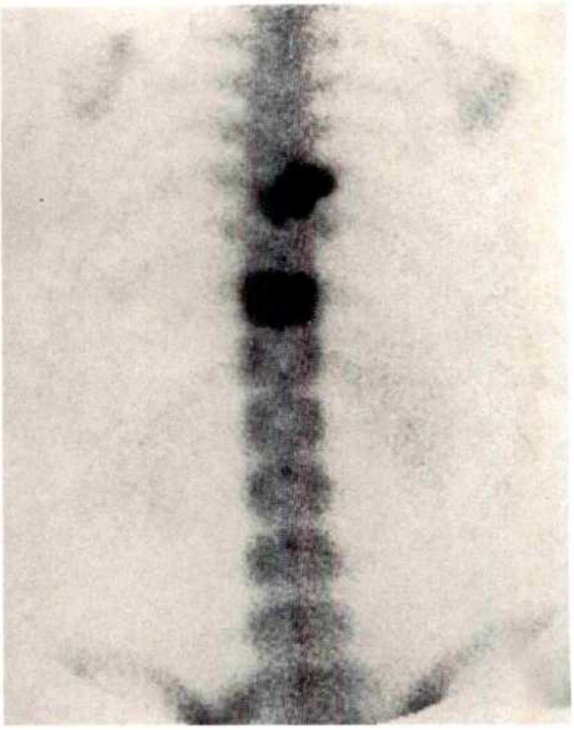

Figure 2. ^{99}Tc^{m}-HMDP bone scintigram showing increased uptake in T9 and T11.

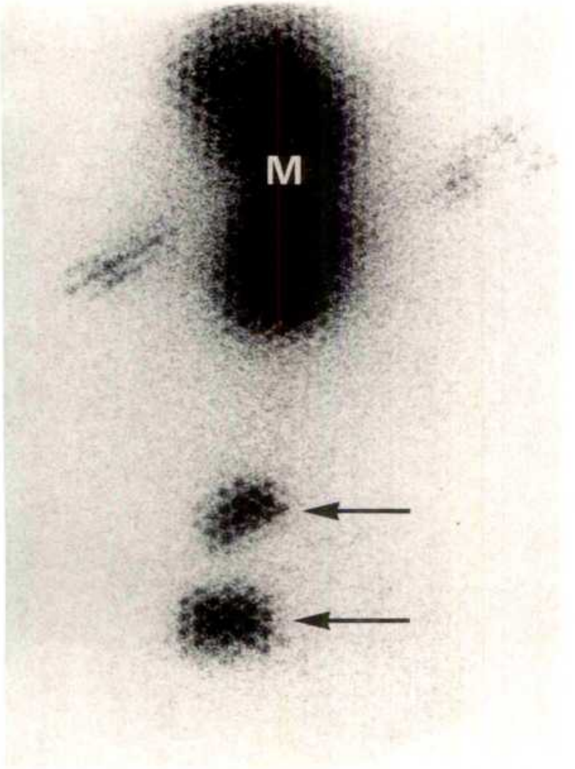

Figure 3. Posterior scan of the thorax after therapeutic administration of ^{131}I-mIBG showing a large amount of uptake in the superior mediastinal mass (M). Uptake is seen in two lower thoracic vertebrae (arrows).

T11 vertebral body. Part of the left 3rd rib was excised and histology showed further malignant tumour. The patient and his family moved districts and further treatment was undertaken at our Centre.

Review of the histology suggested a metastasizing aortico-sympathetic paraganglioma. Subsequent investigations revealed elevated urinary catecholamines although the patient did not demonstrate overt functional symptoms. By this stage the patient had a right supraclavicular mass with tumour extension into the superior mediastinum on plain radiography (Fig. 1) and computed tomography (CT). Bone scintigrams using ^{99}Tc^{m}-HMDP showed metastases in several thoracic vertebrae and the left 4th rib (Fig. 2). A diagnostic mIBG scan using 18 MBq of ^{123}I showed the tumour took up mIBG avidly. Subsequently therapeutic doses of ^{131}I-mIBG were administered (Fig. 3). From 6 July 1988 to 28 November 1989 the patient received three therapeutic doses of ^{131}I-mIBG (1×7.4 GBq and 2×14.8 GBq, respectively). Bone marrow was harvested before the second treatment.

Response to treatment was assessed objectively by the size of the supraclavicular mass, urinary catecholamines and ^{123}I-mIBG and ^{99}Tc^{m}-HMDP scintigrams and subjectively by the patient's symptoms. No significant change in heart rate or blood pressure was observed during or after infusion of ^{131}I-mIBG. Over this period the treatments kept the disease process in check (with marked improvement of bone pain) although little change in any of the objective parameters was observed. However, the metastasis in the T11 vertebral body became sclerotic following treatment, evidence of a positive response. The patient became pancytopenic after the third dose but his marrow soon recovered.

A bone marrow biopsy at this stage showed infiltration by tumour cells. In November 1989 the disease progressed with development of lung metastases and further bone metastases. A further dose of ^{131}I-mIBG (14.8 GBq) was administered, after which the patient developed a prolonged episode of pancytopenia necessitating a series of both blood and platelet transfusions. Bone pain was again controlled although the disease continued to progress. His condition started to deteriorate more rapidly in May 1990 and he received several radiotherapy fractions for painful bony metastases. The patient died in July 1990 after having developed spinal cord compression.

Discussion

mIBG has previously been shown to be effective in the treatment of other neuroendocrine tumours including neuroblastoma, carcinoid and medullary carcinoma of thyroid (Sandler, 1988). The total therapeutic activity of ^{131}I-mIBG given was 51.8 GBq, which is a larger activity than has usually been given for other neuroendocrine tumours (Khafagi et al, 1987; Baulieu et al, 1988). Treatment with ^{131}I-mIBG initially controlled the disease process and considerably reduced bone pain although latterly the disease became more aggressive. Problems were encountered with marrow suppression because of the high doses necessitating control, although when used in lower doses this problem has not been observed (Baulieu et al, 1988). Also in this case the pancytopenia was partly attributable to marrow infiltration by tumour. No changes in either blood pressure or tests of autonomic functions have been observed in a series of patients treated for phaeochromocytomas with mIBG (Sisson et al, 1984), and none were observed in this case. Previous cases of similar malignant paragangliomas of the mediastinum have been treated with surgical resection, radiotherapy and less successfully with chemotherapy (Odze & Begin, 1990) but the rarity of this tumour makes comparative analysis of different treatment methods difficult. It is probably an incurable disease when metastatic, but ^{123}I-mIBG may be useful in its assessment and if this shows uptake by the tumour, ^{131}I-mIBG may be used for treatment.

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^{99}Tc^{m}-HMPAO SPECT and magnetic resonance studies in L-asparaginase induced cerebrovascular accident

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Case report

Symptoms including malaise and fever over an 8 week period prompted the parents of their 14-year-old daughter to seek medical attention. She was found to be pancytopenic and, after a bone marrow aspirate suggested a diagnosis of acute leukaemia, she was referred to St Jude Children's Research Hospital. Her initial white cell count was 1.4×10^9/l. Examination of the cerebral spinal fluid (CSF) showed no white cells or blasts in a cytospin preparation. She was entered on the current front-line protocol for the treatment of children with acute lymphoblastic leukaemia (St Jude total therapy study XII). Induction therapy comprised of daunorubicin, prednisone, vincristine and L-asparaginase, followed by teniposide (VM-26) and cytosine arabinoside (Ara-C) on Day 22. Triple intrathecal chemotherapy with methotrexate, hydrocortisone and cytosine arabinoside was given on Day 2. The patient received six doses of *Escherichia coli* L-asparaginase (Days 3, 4, 6, 8, 10 and 12). After a gynaecology consultation on Day 10, she was started on medroxyprogesterone acetate (Provera) 2.5 mg/day to suppress menstruation during chemotherapy.

On Day 14 of induction therapy the patient had two brief focal seizures, characterized by jerking of the left arm with deviation of the eyes and the head to the left. There was no loss of consciousness. Physical examination revealed a left facial (VII) nerve palsy and weakness of the left arm, but no other abnormalities. The left facial nerve palsy was transient, but the upper extremity weakness persisted for several days. Her platelet count was 67×10^9/l, prothrombin time was 23.4 s (control 12.1), partial thromboplastin time was 35.6 s (control 24.4), and fibrinogen was 16 mg/dl (normal 150–400).

An emergency computed tomography (CT) scan was performed, (Fig. 1a & b), which showed a 1.5 cm rounded area of increased attenuation in the left parieto-occipital lobe junction, consistent with a focal intracerebral haematoma. There was a thin rim of oedema, but no significant mass effect. No lesion was seen in the right cerebral hemisphere.

The results did not explain the clinical findings, therefore, a single photon emission computed tomography (SPECT) scan was performed on the same day. After the administration of ^{99}Tc^{m} (Ceretec, a radionuclide agent (HMPAO)), an anterior flow study of the head was performed and 64 (20 s) images were obtained (Fig. 2). Small perfusion defects were evident in the upper convexities of both the right fronto-parietal and left parieto-occipital regions. The lesion on the left corresponded to that seen on the CT scan. These findings were interpreted as bilateral small vessel thromboses.

A magnetic resonance imaging (MRI) examination was performed the following day using proton density, T_2, gradient echo phase and pre- and post-contrast T_1 images. The left haematoma was seen easily (Fig. 3a) with evidence of haemosiderin deposits on gradient echo phase images. The lesion in the right pre-central gyrus showed increased proton density and T_2 signal intensity (Fig. 3b), without evidence of methaemoglobin or haemosiderin.

The patient was treated twice with fresh frozen plasma 10 ml/kg in the first 24 h. The clotting time returned to normal. She also received a short course of steroids (dexamethasone 4 mg every 4 h) and was started on phenobarbital. The strength in her left arm returned to normal within 72 h of the seizure. Maintenance phenobarbital was continued. A bone marrow, performed the day after her seizures, showed 8% residual blasts. Three additional doses of L-asparaginase were

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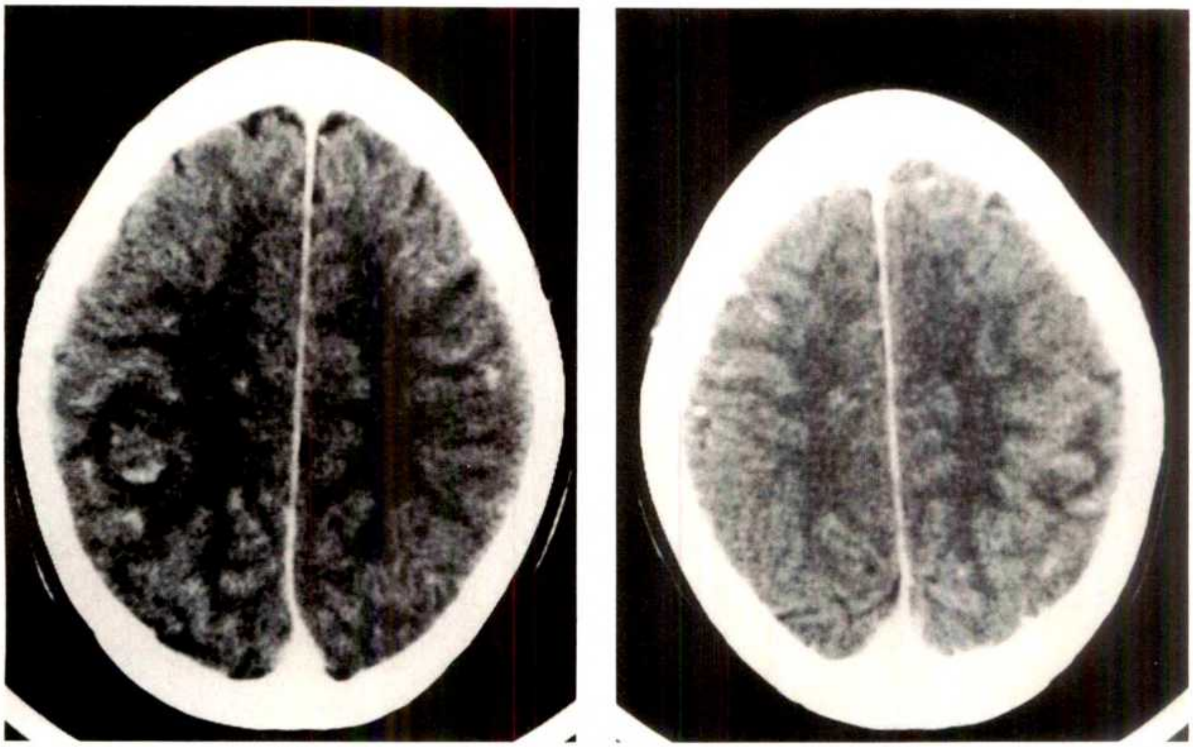
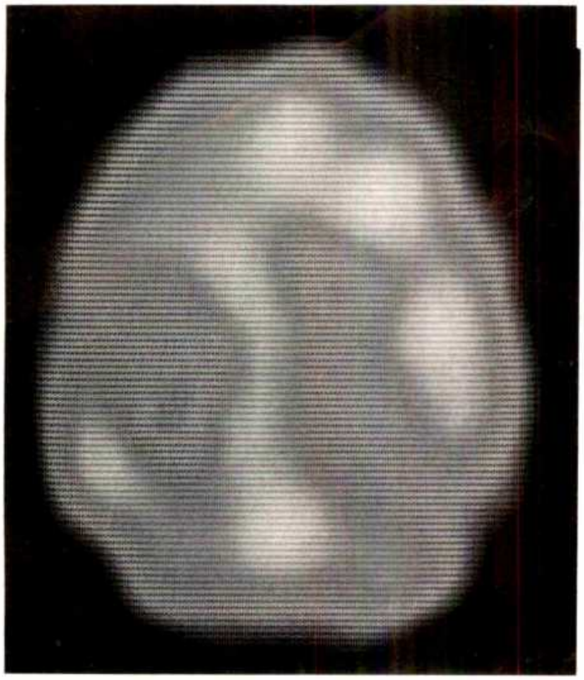


(a) (b)

Figure 1. Cranial CT on day of cerebrovascular accident (CVA). (a) Lower level, with contrast, demonstrating left cerebral CVA. (b) Upper level, with contrast, showing no lesion in the right hemisphere.



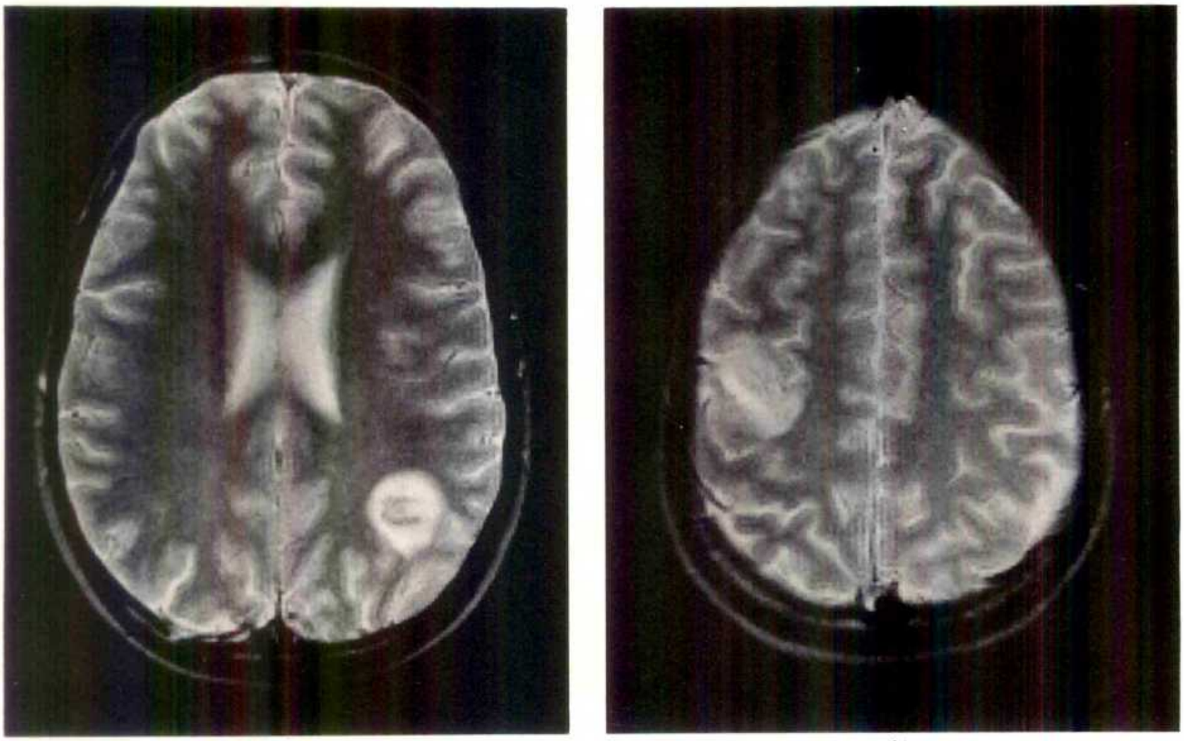
omitted because of the cerebrovascular insult and were replaced by an additional dose of daunorubicin.

A follow-up SPECT scan 2 weeks later showed improvement, but minimal perfusion defects were still noted in both previously abnormal areas. An MRI scan performed 4 weeks after the insult also showed improvement, but was still abnormal in both areas. The patient remains clinically well, without abnormal neurological signs. She has had no further seizures over a 6 month period.

Discussion

The use of L-asparaginase during remission induction therapy is associated with coagulation abnormalities that can result in cerebral thrombosis or haemorrhage (Priest et al, 1982; Kucuk et al, 1985; Packer et al, 1985). The coagulation abnormalities associated with L-asparaginase include prolonged prothrombin and partial thromboplastin times and decreased fibrinogen, factor IX, von Willebrand factor, antithrombin III and proteins C and S (Homans et al, 1987; Pui et al, 1987;

Figure 2. Thick transverse SPECT image on the day of CVA demonstrating decreased activity (blue) in the left parietal-occipital lobes in the same area as the lesion shown on CT (Figs 1a & b) and MRI (Fig. 3a), and in the right fronto-parietal lobes as shown on MRI (Fig. 3b), but not on CT.



(a) (b)

Figure 3. Cranial MRI 1 day after CVA and CT. (a) T_2-weighted image of lower level (same as Fig. 1a & b) demonstrating left cerebral CVA. (b) T_2-weighted image of upper level showing oedematous right cerebral CVA.

Saito et al, 1989). Although coagulation defects are seen in all patients given multiple doses of L-asparaginase, only 1–2% have cerebral thrombosis or haemorrhage. These cerebral events occur most commonly in the second or third week of therapy, as in our patient (Priest et al, 1982).

In our patient, the only extra potential risk factor for thrombosis was the administration of the progesterone derivative Provera for 4 days before her cerebral event. There is a suggestion that arterial thrombosis can result from progesterones (Meade et al, 1980). However, menstruation during a period of thrombocytopenia and deranged coagulation is associated with an increased risk of excessive bleeding.

Presumably, bilateral small vessel thrombosis with resulting ischaemia was the primary cerebral insult. Secondary haemorrhage occurred only in the left hemisphere. A CT scan showed the secondary haemorrhage on the left side but not the ischaemia on the right. Thrombosis on the right side was more anterior and, therefore, affected the motor cortex, whereas the left-sided event was clinically silent. In Priest's description of cerebral events after L-asparaginase, CT scans were initially normal in eight of 14 patients and remained normal in three (Priest et al, 1982). Moreover, Priest described three patients whose CT scans were normal, although the patients were symptomatic. 2–5 days later these patients developed lesions, on repeat CT scan, indicative of intracranial blood. It can be speculated that the underlying problem was small vessel thromboses that could not be detected by initial CT scans. Secondary haemorrhage after thrombosis may result in a lesion on the CT scan without demonstrating the initial thrombotic lesion.

In our patient MRI clearly showed the ischaemic lesion in the right motor strip. Schick et al (1989) reported that MRI was a rapid, effective means of demonstrating dural sinus thrombosis, secondary to L-asparaginase therapy. HMPAO-SPECT has been shown to be useful in the rapid demonstration of perfusion deficits in the first 12 h after cerebrovascular accident in adults, when CT may still be normal (Biersack et al, 1990). This case report extends Schick's finding by demonstrating the utility of MRI in detecting small vessel thrombosis and it shows the usefulness of SPECT scanning in the rapid diagnosis of such a thrombotic event after L-asparaginase.

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Renal arterial fibromuscular dysplasia: acute renal infarction in three patients with angiographic evidence of medial fibroplasia

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Keywords: Renal infarction, Fibromuscular dysplasia, Renal angiography

Fibromuscular dysplasia of the renal arteries usually presents with hypertension but, rarely, it can present with acute renal infarction. Of the four types of fibromuscular dysplasia, medial fibroplasia has been said not to progress to renal arterial occlusion (Schreiber et al, 1984) and not to predispose to arterial thrombosis or dissection (Stewart et al, 1970).

We report on three patients who presented with acute renal infarction, whose renal angiographic features were more suggestive of the medial fibroplasia type of fibromuscular dysplasia.

Case reports

Case 1

A 33-year-old man was admitted with severe right loin pain. The right kidney was non-functioning on intravenous urography, but an ultrasound examination of both kidneys was normal. A right retrograde pyelogram was normal, but dynamic renography (^{99}Tc^{m}-DTPA) revealed that the right kidney was not perfused.

At angiography the right renal artery was completely occluded by thrombus 3 cm from its origin (Fig. 1). The left main renal artery was irregular and two stenoses were seen in one of the segmental vessels (Fig. 2). The thrombus in the right main renal artery was treated with intra-arterial streptokinase to reveal a 75% stenosis. This was treated with balloon angioplasty but peripheral perfusion could not be restored and the kidney remained non-functioning. The angiographic appearances were thought to represent the medial fibroplasia form of fibromuscular dysplasia. Subsequent investigations failed to reveal any other cause of arterial thrombosis or embolism.

Case 2

A 33-year-old man was admitted with a 5 day history of severe left loin pain. No abnormality was detected on intravenous urography but static renography (^{99}Tc^{m}-DMSA) demonstrated absence of activity in the lower lateral part of the left kidney, which was suggestive of renal infarction. There was a smaller cortical defect in the right kidney.

Renal angiography revealed a series of strictures and dilatations of the arteries supplying the lower pole of the left kidney. One segmental artery was occluded (Fig. 3). The right main renal artery was irregular and strictures and dilatations were seen in a segmental artery which was occluded distally

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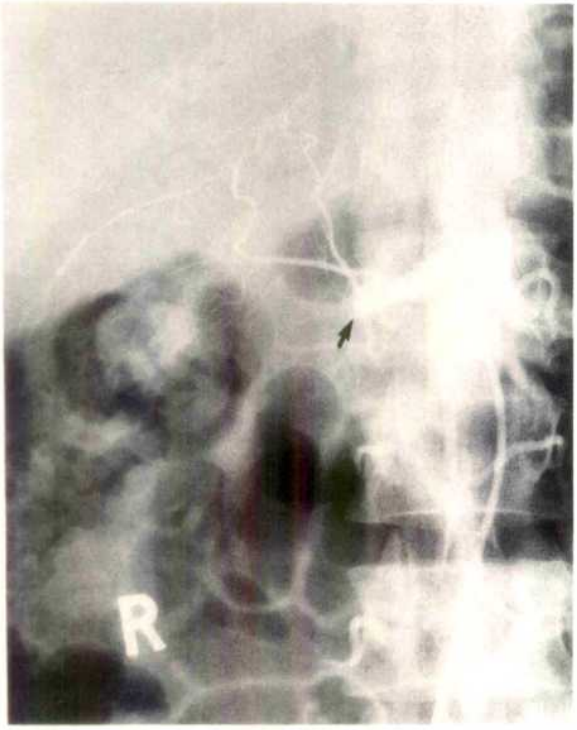

Figure 1. Case 1. Flush aortogram. The right renal artery is occluded by thrombus.

(Fig. 4). The superior mesenteric artery was also irregular (Fig. 5). Although the appearances in the left renal artery were not typical, the overall impression was of a diagnosis of medial fibroplasia.

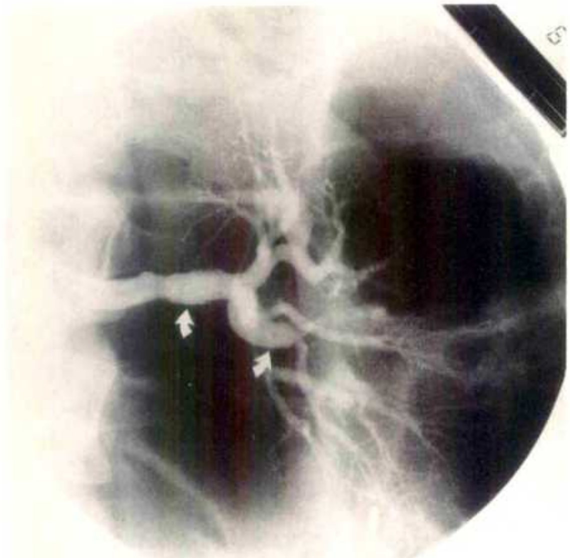

Figure 2. Case 1. Selective left renal arteriogram. An irregular left main renal artery with aneurysmal dilatations and strictures of a segmental artery.

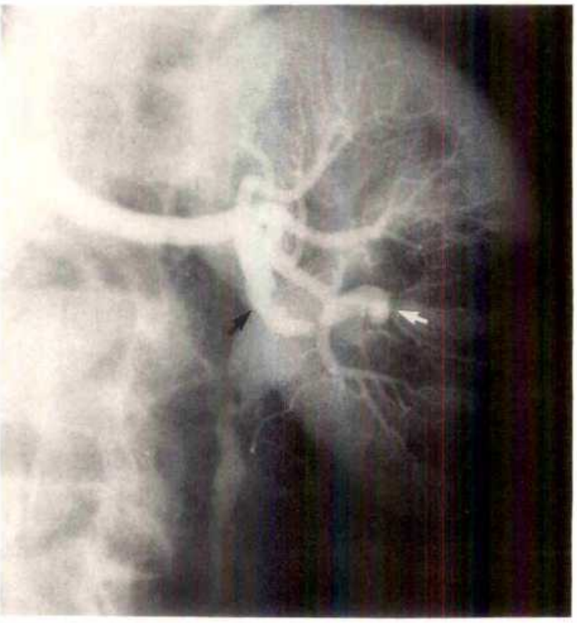

Figure 3. Case 2. Selective left renal arteriogram. Aneurysmal dilatations and strictures of the artery supplying the lower pole of the left kidney. A segmental artery is occluded.

Case 3

A 34-year-old man was admitted with a 3 day history of left loin pain. No abnormality was detected on intravenous urography but dynamic renography (^{99}Tc^{m}-DTPA) showed a wedge-shaped defect in the midpole of the left kidney, highly suggestive of renal infarction.

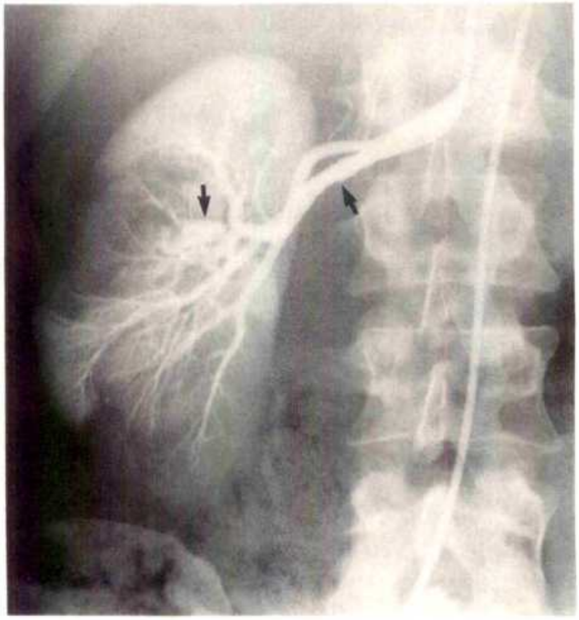

Figure 4. Case 2. Selective right renal arteriogram. Irregularity of the right main renal artery. Strictures and dilatations are seen in a segmental artery which is occluded distally.

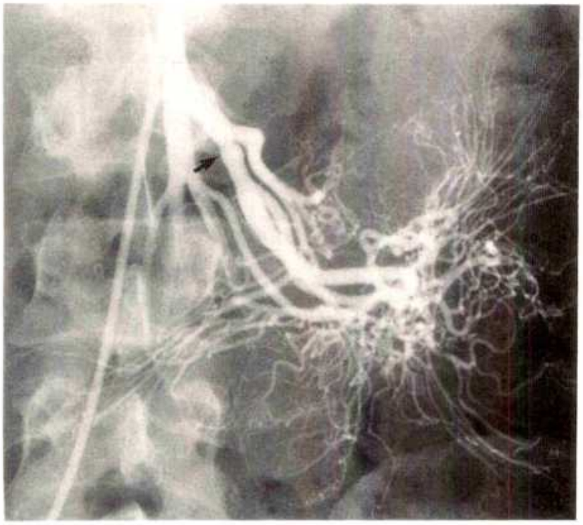

Figure 5. Case 2. Selective superior mesenteric angiogram. There are strictures and dilatations of the superior mesenteric artery.

Renal angiography revealed an occluded branch artery to the middle pole of the left kidney (Fig. 6). The typical appearance of medial fibroplasia was seen in the distal part of the right main renal artery (Fig. 7). No other cause of arterial thrombosis or embolism was discovered on detailed investigation.

Discussion

The term fibromuscular dysplasia refers to a group of conditions of unknown aetiology which cause non-atheromatous arterial stenoses. Four distinct histological types have been described: intimal fibroplasia, true fibromuscular hyperplasia, medial fibroplasia and perimedial fibroplasia (Stewart et al, 1970).

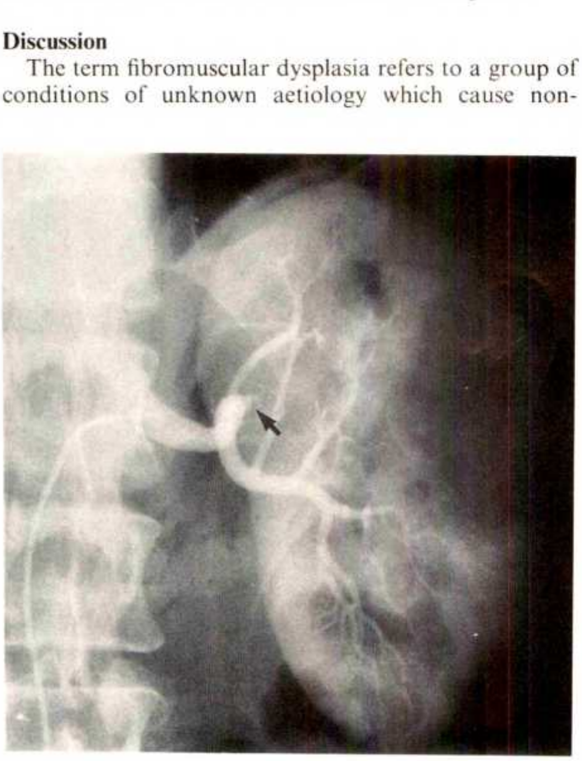

Figure 6. Case 3. Selective left renal arteriogram. There is stenosis proximally in a segmental vessel which is occluded distally.

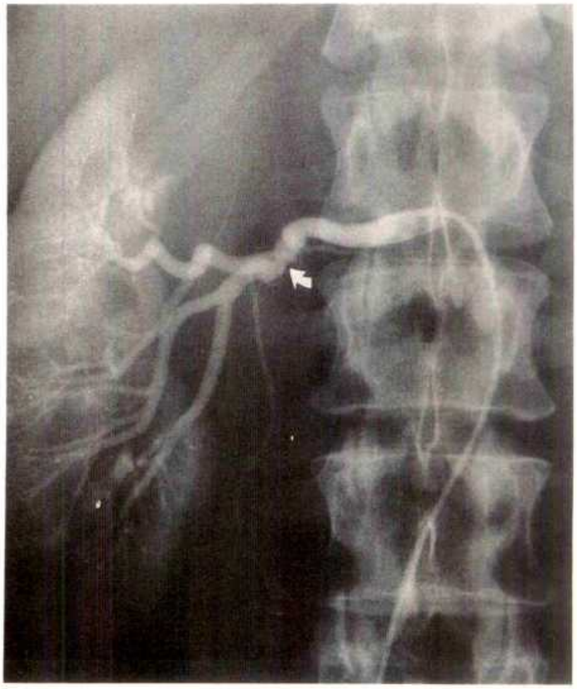

Figure 7. Case 3. Selective right renal arteriogram. The "string of beads" appearance of medial fibroplasia is seen in the distal right main renal artery.

Intimal fibroplasia and true fibromuscular hyperplasia cannot be distinguished from each other clinically or angiographically. Both are conditions of children and young adults in whom smooth, focal stenoses are seen in the renal arteries (Stewart et al, 1970). Medial fibroplasia is by far the most common type of fibromuscular dysplasia, accounting for 75% of all cases. It is predominantly a disease of young women and a "string of beads" appearance is characteristically seen on angiography. This appearance is caused by a series of fibrous strictures interspersed with aneurysmal dilatations of the artery. Perimedial fibroplasia is also a disease of young women in which the arteries have a beaded appearance. It is distinguished angiographically from medial fibroplasia because the "beads" are smaller than the diameter of the normal artery (Stewart et al, 1970).

In all three cases, the irregular appearance of the main or segmental renal arteries was caused by the presence of a series of stenoses interspersed with dilatations of the artery. This appearance is more typical of medial fibroplasia which occurs five times more frequently in females. Interestingly all three cases were male.

It has been said that medial fibroplasia does not predispose to arterial thrombosis or dissection (Stewart et al, 1970). Schreiber et al (1984) followed 66 patients with medial fibroplasia for 45 months and found that although some lesions became more stenotic, none progressed to complete arterial occlusion. Meaney et al (1968) reported one patient with medial fibroplasia, who developed complete thrombosis of the renal artery. However, this case was complicated by the presence of an atheromatous plaque at the origin of the artery. Goncharenko et al (1981) described two further cases of renal infarction secondary to medial fibroplasia.

Renal arterial occlusion is a recognized complication of the other types of fibromuscular dysplasia. It is most frequently associated with perimedial fibroplasia, either as a result of arterial thrombosis or simply caused by progression of the disease. Both intimal fibroplasia and true fibromuscular hyperplasia predispose to arterial dissection which can also lead to renal infarction.

It has been suggested that because the risk of renal infarction is low in medial fibroplasia, percutaneous angioplasty should be reserved for those patients with refractory hypertension (Schreiber et al, 1984). Early renal revascularization is recommended for patients with the other types of fibromuscular dysplasia because of the rapidly progressive natural history of these conditions and the high risk of subsequent renal infarction (Stewart et al, 1970). We have demonstrated that such fine distinctions are unsafe and that perhaps all patients with renal arterial fibromuscular dysplasia are at risk of renal infarction.

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1992, *The British Journal of Radiology*, 65, 85–86

Case of the month

A persistent offender

By D. Kinsella, FRCR and P. Norman, FRCR
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(*Received 28 November 1990 and in revised form 29 January 1991, accepted 22 February 1991*)

A 28-year-old lady presented with a 12 hour history of severe occipital headache. The onset of the headache was sudden. On examination there was mild neck stiffness with no focal neurological signs. The initial radiological examination was a head computed tomography (CT) scan which demonstrated a recent subarachnoid haemorrhage. The following day cerebral angiography was performed (Fig. 1).

What abnormalities are shown and what is the diagnosis?

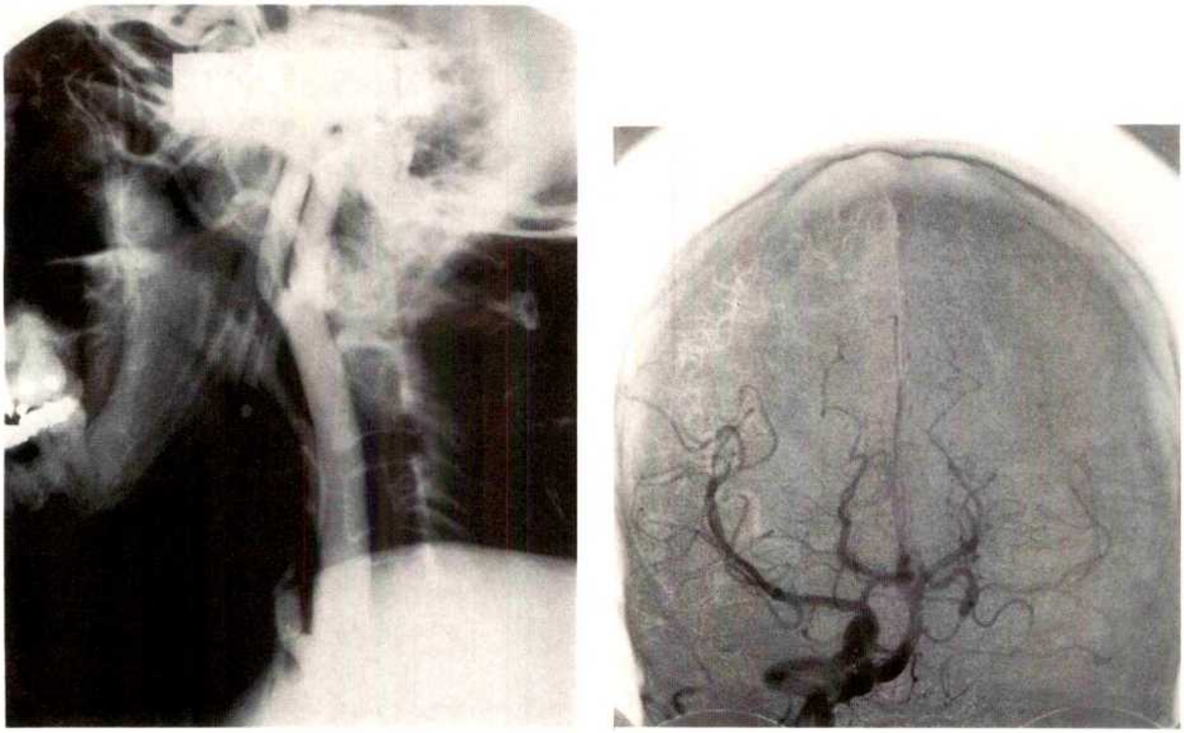
(a) (b)

Figure 1. Two views from the right common carotid arteriogram: (a) lateral cervical and (b) AP cranial.

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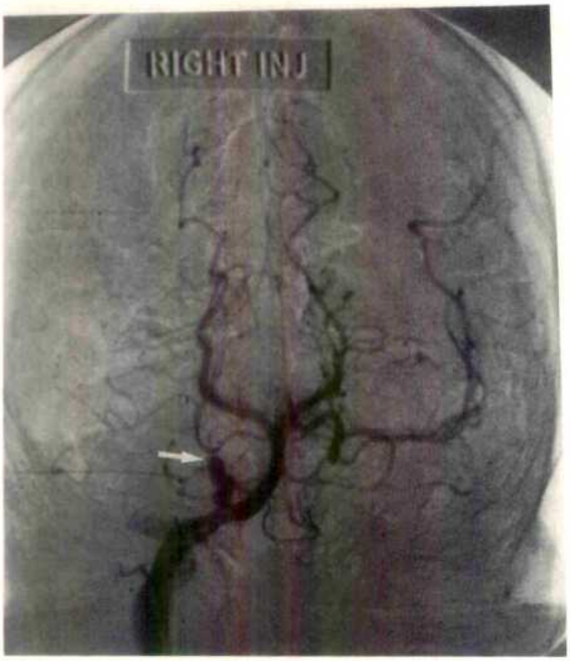

Figure 2. Selective hypoglossal artery injection showing the aneurysmal sac (arrow).

The right common carotid arteriogram demonstrates a communication between the right internal carotid and the basilar arteries. This is caused by a persistent hypoglossal artery. The hypoglossal artery has a large aneurysmal sac close to its termination in the basilar artery. The sac is projected behind the terminal portion of the right internal carotid artery in Fig. 1b. It can be identified clearly following a selective hypoglossal artery injection (Fig. 2). There is no retrograde filling of the distal portions of the vertebral arteries following this injection. The origins of the vertebral arteries could not be determined following selective injections into the innominate and left subclavian vessels.

Discussion

During fetal life, prior to the development of the vertebral system, there are multiple anastomoses between the internal carotid artery and the basilar artery. Usually these anastomoses only function until the end of the first week of post-natal life (Brismar, 1976). However, they may persist as the trigeminal, the hypoglossal or the acoustic arteries (Fig. 3). The first angiographic report of a persistent trigeminal artery was published by Sutton (1950). This vessel arises from the internal carotid artery as it enters the cavernous sinus and passes posteriorly to join the basilar artery. In a large angiographic series the frequency of this abnormality is between 0.1 and 0.2% (Lie, 1968). The persistent hypoglossal artery arises from the cervical portion of the internal carotid artery at C1 or C2. It enters the skull via the hypoglossal canal and terminates as the basilar artery. In the presence of a persistent hypoglossal artery the vertebral arteries are frequently hypoplastic (Brismar, 1976).

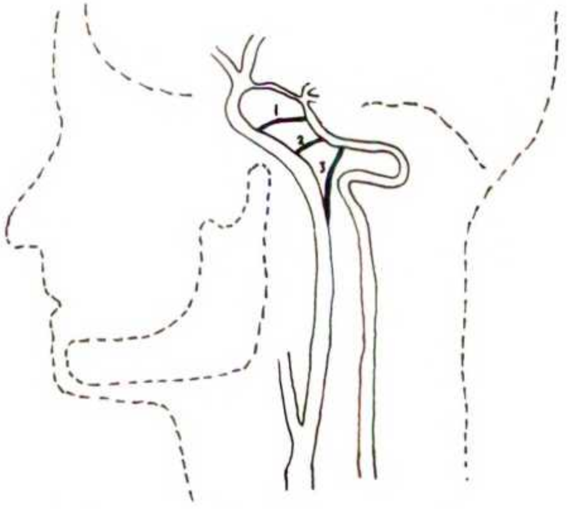

Figure 3. Sites of persistent fetal arteries connecting the right internal carotid artery and the basilar artery: (1) primitive trigeminal artery; (2) primitive acoustic artery and (3) primitive hypoglossal artery.

Less than 5% of cerebral aneurysms occur in the vertebro-basilar system. Although a persistent hypoglossal artery is a rare anomaly, several cases indicating an association with aneurysm formation have been reported (Udvarhelyi & Lai, 1963; Huber & Rivoir, 1974). The altered haemodynamic state at the junction of the large persistent hypoglossal artery and the smaller basilar artery could result in weakening of the vessel wall leading to aneurysm formation.

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Keywords: Hypoglossal artery aneurysm, Subarachnoid haemorrhage

1992, *The British Journal of Radiology*, *65*, 87–90

Short communication

Carbogen breathing: a system for use in man

By S. Dische, *A. Rojas, T. Rugg, A. Hong and *B. D. Michael

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(*Received 2 April 1991 and in revised form 22 May 1991, accepted 13 June 1991*)

Keywords: Hypoxic cell radiosensitizer, Carbogen, Clinical trial

In the long history of the clinical application of laboratory knowledge concerned with the radioresistance of hypoxic tumour cells, carbogen ($95\%O_2 + 5\%CO_2$) was employed at an early time. In a randomized controlled trial of carbogen breathing in 254 patients with carcinoma of the upper aero-digestive system, initiated in 1972 and performed under the auspices of the radiation therapy oncology group (RTOG), a small margin of advantage to carbogen breathing in carcinoma of the larynx (total of 42 cases) and hypopharynx (total of 39 cases), which did not reach statistical significance, was reported by Rubin et al (1979). The method fell into disuse and in the 1960s and 1970s the clinical effort was concentrated on hyperbaric oxygen (HBO). Finally there was a move to chemical sensitizing agents.

Recently, using clinically relevant dose-fractionation regimes, it has been shown that both carbogen and 100% oxygen-breathing in mouse tumour models give a remarkable increase in radiosensitivity. The enhancement of radiation effect is greater than that achieved by any other system for sensitization of hypoxic cells in the laboratory, including the use of chemical sensitizers and hyperbaric oxygen (Rojas et al, 1990; Rojas, 1991). The benefit is maintained in multifraction treatments up to 36 fractions and is greater than for single doses. This, together with the more recent evidence that a combination of carbogen and nicotinamide (the amide derivative of vitamin B_3) is an even more effective radiosensitizer combination (Kjellen et al, 1991), has led to a revival of interest in carbogen breathing for clinical application.

The long period of up to 2 h between initiation of carbogen breathing and radiotherapy, as employed in two early clinical trials (Rider et al, 1969; Rubin et al, 1979), can be questioned. In our mouse tumour models, radiotherapy commences shortly after the onset of carbogen administration and maximum increase in radiosensitivity is seen following a 5 min pre-irradiation breathing interval. Furthermore, others have shown that radiosensitization in experimental tumours markedly decreases if too long a pre-irradiation interval is used (Suit et al, 1972; Siemann et al, 1977). There is evidence that maximum increases in pO_2 were reached in some human tumours after short periods of exposure (5–10 min) to either carbogen or oxygen (Cater & Silver, 1960; Kolstad, 1964). However, others have reported that longer intervals of $\geqslant$ 20 min are required, but anaesthesia was employed and HBO was under test (Evans & Naylor, 1963). Prolonged exposures to high oxygen concentrations can trigger compensatory vasoconstriction and a reduction in blood flow, which may negate the benefit of using these gases (Bird & Telfer, 1965; Guyton, 1984).

We have developed a system for the administration of carbogen and performed a pilot study in eight patients treated by radiotherapy for advanced malignant disease.

Method

Some indication as to the interval which should elapse, after initiation of 100% oxygen or carbogen breathing, may be gained from observing the change in the saturation of oxyhaemoglobin (HbO_2) in a limb and/or by measuring pO_2 in venous blood, as a function of time after institution of carbogen or oxygen. We tested this in one volunteer using near infrared spectroscopy (Delpy et al, 1987) and in five volunteers by serial determinations of venous pO_2 whilst breathing oxygen, carbogen or air. With both methods rapid increase in HbO_2 and pO_2 were seen within 1–2 min of starting to breathe carbogen or oxygen and maximum concentrations were reached in all cases within 3–10 min. These observations gave support for the use of short intervals between the onset of carbogen breathing and radiotherapy. However, we have no direct data concerning the changes which may occur in tumours.

In order to prevent patients inhaling air during carbogen administration, a mouth "gag", as used by scuba divers, was found to be highly efficient in sealing the lips and the nose clip employed was equally effective. The delivery system used incorporated a one-way valve and a gas reservoir. A Phase I study was undertaken in seven patients treated for advanced carcinoma of the bronchus and in one patient for a recurrent malignant melanoma in the leg. All patients gave their informed consent. The dose and fractionation employed in these cases were those generally used at our centre for long term palliation; 6 fractions were given over 19–22 days. A linear accelerator, generating 5 MV X rays was employed in Cases 1 to 7, and 250 kV X rays in the last case. The normal dose used in these patients was reduced by 5% in those cases where the spinal cord was included in the target volume, thus allowing for a small increment in normal tissue effect suggested from the animal studies. Table I summarizes the clinical features of each patient and the radiotherapy given.

Carbogen breathing was commenced as soon as the patient reached the treatment room and intervals from initiation of carbogen breathing to onset of radiotherapy ranged from 4 to 7 min. Treatment times ranged from 10 to 20 min, depending on the number of fields and the apparatus employed. Therefore, the total duration of gas breathing was between 14 and 27 min. In these patients no problems were encountered in positioning or set-up for radiotherapy.

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Table I. Clinical features and radiotherapy employed

Case number	Sex	Age	Diagnosis	Extent of disease	Radiotherapy			Technique
					dose (Gy)	number of fractions	overall time (days)	
1	M	61	moderately differentiated squamous cell carcinoma (SCC) bronchus	4 cm diameter mass left hilum. CT: ?hepatic metastases	33 (min)	6	21	4 field plan
2	M	35	poorly differentiated SCC bronchus	5 cm diameter mass right hilum. Mediastinal and left scalene nodes	35 (max)	6	21	anterior and right posterior oblique
3	M	55	poorly differentiated SCC bronchus	3 cm diameter mass right hilum. CT: pleural nodes over right lung	35 (max)	6	19	4 field plan
4	M	50	poorly differentiated adenocarcinoma bronchus	peripheral mass left upper lobe destroying 3rd rib. Mediastinal nodes	30. 4 (max)	6	22	pair opposing
5	M	60	SCC bronchus	6 cm diameter mass right hilum. Small pleural effusion blood stained; cytology negative	33.2 (min)	6	20	4 field plan
6	M	55	poorly differentiated SCC bronchus	3 cm diameter mass right hilum. Mediastinal and left scalene nodes	30.4 (min)	6	19	pair opposing
7	M	74	poorly differentiated SCC bronchus	8 cm diameter mass left upper lobe invading chest wall	33.2 (max)	6	19	anterior and left posterior oblique
8	F	50	malignant melanoma lower leg (surgery)	32 mm diameter scalene deposit ~ 20 mm deep, in posterior calf	32 (midline)	6	21	opposing fields 250 kVp

Results

All eight patients found the system entirely acceptable and all treatments given were completed exactly as planned. Early reactions were similar to those normally seen with the dose/fractionation regime.

The patients showed a variety of responses of their advanced tumours and these are summarized in Table II. The clinical objective of long term palliation was well served in these patients. Apparent, complete regression was observed in four patients which remained to death at 6 and 20 months in two cases while two patients are alive 2 years after treatment. However, in routine practice long term control may be achieved with the scheme of radiotherapy employed. It should be noted that one patient, with a remarkably good response in a carcinoma showing extensive rib destruction, subsequently showed radiation myelitis. The dosage in spinal cord was recalculated and was confirmed to be at a level considered, by long experience, safe and was more than 10% lower than that which has been associated with myelitis (Dische et al, 1988). The patient who received carbogen breathing while undergoing radiotherapy to the lower leg in the treatment for recurrence of malignant melanoma showed complete regression and healing. However, 18 months later there was breakdown of skin and a necrotic ulcer appeared. This patient subsequently had a skin graft performed of the area which is now well healed and remains free of tumour.

Discussion

The technique of treatment appears to be a highly practical one. The episodes of radiation myelitis and of skin breakdown suggests an increment of effect in normal tissues greater than predicted. However, in the RTOG study there was no significant difference in the complication rate between patients treated in air or carbogen (Rubin et al, 1979). Late radiation effects in the spinal cord are known to be increased by radiotherapy with HBO and reduced when the haemoglobin level is in the lower portion of the normal range (Coy & Dolman, 1971; Dische et al, 1988), indicating that the cord is a structure where radiosensitivity may be readily altered by pO_2 changes. In skin, radiosensitivity may be modified greatly by external conditions such as temperature and the lower leg is known to be a site susceptible to radiation damage. In addition, treatment was given using an orthovoltage apparatus and no relative biological effectiveness compensation was applied.

The technique for administering carbogen to patients seems

Table II. Treatment outcome in patients breathing carbogen during radiotherapy

Case number	Response of treated tumour	Subsequent course	Alive/dead	Time to death or last seen (months)
1	Complete regression as assessed by chest X ray	liver and bone metastases. No evidence for local recurrence	dead due to metastases	6
2	Partial regression small residium seen in chest X ray	local recurrence at 8 months. Subsequently liver metastases	dead due to local and distant disease	12
3	?Complete regression X ray difficult to assess due to pleural disease	extensive pleural disease at 5 months symptomatic at 8 months	dead due to extensive intrathoracic tumour	16
4	Complete regression as assessed by chest X ray	radiation myelitis at 6 months complete paraplegia	dead, no definite tumour recurrence	20
5	Complete regression as assessed by chest X ray	well, some shortness of breath	alive, no evidence of tumour	25
6	Partial regression as assessed by chest X ray	abdominal mass at 3 months. Laparotomy: inoperable bowel tumour	dead due to abdominal tumour	3
7	Partial regression as assessed by chest X ray	symptomatic relief but evidence of local regrowth and widespread metastases. at 5 months	dead due to local and distant disease	6
8	Complete regression and healing	chemotherapy for multiple deposits. Skin ulceration at 18 months. Excised and grafted successfully; no tumour	alive but on systemic therapy for multiple metastases	24

to be a practical one, but reductions of dose are required when tissues likely to show enhanced response with carbogen, such as skin and spinal cord, are included in the treatment field.

Acknowledgments

We wish to thank Mrs C. Thorn of the Department of Physics and Bio-engineering, University College London, for performing the oxyhaemoglobin measurements and Mr P. Lockwood, of the Respiratory Physiology Department, Harefield Hospital, for determining the pO_2 measurements. This work was partly funded by the Cancer Research Campaign.

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1992, *The British Journal of Radiology*, 65, 91

Erratum

The Editor—Sir,

In a paper entitled "Patient doses from computed tomography in Manitoba from 1977 to 1987" by W. Huda et al (1989), there is an error in equation 2 on page 140. The revised equation 2 should read

$$H_E(X) = H_E(\mathrm{EMI}) \frac{R(X) \,.\, N(X) \,.\, [T(X)]^2 \,.\, \mathrm{mAs}(X)}{R(\mathrm{EMI}) \,.\, N(\mathrm{EMI}) \,.\, [T(\mathrm{EMI})]^2 \,.\, \mathrm{mAs}(\mathrm{EMI})} \qquad (2)$$

This change (*i.e.* replacing the slice thickness T by the slice thickness squared T^2) requires modification of the resultant Tables V, VI and VII.

The modified Table V should now read

Scanner	Examination type (Average H_E value in mSv)			
	Head	Chest	Abdomen	Pelvis
EMI 5005	0.84	4.8	2.6	2.1
GE 9800	1.5	12.1	4.9	5.1
Siemens DRH	1.4	9.9	5.9	8.1

The corrections for Table VI are only for the years 1984 to 1987. In these years, the collective effective dose equivalent has been overestimated by factors which range from 10% to 30%. The (approximate) corrections for these years are given below.

1984 10% reduction in the collective dose (person-Sv)
1985 15% reduction in the collective dose (person-Sv)
1986 15% reduction in the collective dose (person-Sv)
1987 30% reduction in the collective dose (person-Sv)

In Table VII, the computed average H_E values for patients undergoing CT scans in Manitoba are obtained using the collective dose values given in Table VI. Thus the values of average patient H_E for the years 1984 through 1987 should be reduced by the same amount as the collective doses in Table VI. In addition, in Table VII the correct scanner specific patient H_E values should now read:

Average patient H_E for the GE scanner (1987)	3.1 mSv
Average patient H_E for the Siemens DRH	3.4 mSv

Yours etc.,

W. Huda
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(*Received 9 September 1991*)

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Huda, W., Sandison, G. A. & Lee, T. Y., 1989. Patient doses from computed tomography in Manitoba from 1977 to 1987. *British Journal of Radiology*, 62, 138–144.

1992, The British Journal of Radiology, 65, 92–95

Correspondence

(The Editors do not hold themselves responsible for opinions expressed by correspondents)

Dosimetric accuracy at low monitor unit settings

The Editor—Sir,

I read with interest the article by Das et al (1991) and appreciate the authors' concern over the accuracy of dosimetry systems at high dose rates and low monitor unit settings.

The purpose of writing this letter is to underline that, in the UK, the accuracy of patients' treatments should not be jeopardized as suggested, in that short exposures on linear accelerators have been deprecated for the past 20 years (HMSO, 1972; DHSS, 1975; NRPB, 1988). Where low monitor unit settings are required, then the recommendation is that the dose rate should be reduced to increase the exposure time to at least 20 s; a practice endorsed by Barish et al (1987). Unfortunately, Das et al do not appear to have considered the beam instability of servo-controlled accelerators during, say, the first 5 s of the exposure in their analysis (Barish et al, 1987; Tuohy & Morgan, 1990)

Yours etc.,
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(Received 10 April 1991, accepted 23 July 1991)

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Barish, R. J., Fleischman, R. C. & Pipham, Y. M., 1987. Teletherapy beam characteristics: the first second. *Medical Physics, 14*, 657–661.

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Tuohy, J. B. & Morgan, A. M., 1990. Temporary enlargement of penumbra on linear accelerators. *British Journal of Radiology, 63*, 911.

Authors' reply

The Editor—Sir,

In his letter, Bomford has pointed out some concerns about our recent paper, Das et al (1991). Let us state that in the paper we do not suggest that typical patient's treatments are likely to be jeopardized because of low monitor unit settings. In fact, we state in the conclusions that "...in terms of total target dose, the error may be insignificant. Only when the treatment is made up of small MU exposures..." is the error possibly of significance. This situation should arise only rarely, but the user should be aware of the potential for error. Increasing the exposure time may be one of the ways to reduce the error, but this requires reducing pulse repetition frequency (PRF) which may not be readily achievable with all medical accelerators.

One cannot say, as Bomford does, that reducing the dose rate is "a practice endorsed by Barish et al (1987)". Barish et al stated that they were able to reduce the variation in beam energy, flatness and symmetry at low MU by lowering the PRF, *i.e.* lowering the dose rate, on a Philips SL75-20. However, they did not investigate the same effect on other accelerators, nor did they investigate accuracy of delivered dose. Reducing the dose rate may not be as simple as reducing the PRF on all units, *e.g.* a CGR Saturne where the dose rate is adjusted by changing the beam current at a constant PRF. Also, with most accelerators, a change in dose rate, as suggested, would require by-passing one or more critical safety interlocks which is not recommended. We think that it is not a procedure to be carried out routinely.

In response to Bomford's comment about neglecting to consider beam instability, let us point out that in the discussion, paragraph 3, we acknowledge that instabilities caused by the servo control could be related to the problems caused by beam instability, and reference Barish et al (1987). Our primary purpose was to emphasize the potential problem caused by variations in the dose per monitor unit and caution users to understand their equipment relative to the demands of patient treatments, quality control and dosimetry.

Yours etc.,
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References:

Das, I. J., Kase, K. R. & Tello, V. M., 1991. Dosimetry accuracy at low monitor unit settings. *British Journal of Radiology, 64*, 808–811.

Barish, R. J., Fleischman, R. C. & Pipman, Y. M., 1987. Teletherapy beam characteristics: the first second. *Medical Physics, 14*, 657–661.

The effect on pulmonary function of tangential field technique in radiotherapy for carcinoma of the breast

The Editor—Sir,

I am concerned that the paper by Lund et al (1991) ends with a bald conclusion that "this technique (lumpectomy followed by tangential field radiotherapy) is a safe procedure in breast-preserving treatment". This should have been qualified by "in patients with normal lung function", since this was the group which they investigated. The damage due to radiation is not reversible. The initial functional abnormalities after radiation are caused by the effect of the continuing perfusion of the damaged areas. In due course, these parts collapse and in healthy patients the remaining lung compensates, with return of function test results to the normal range (the majority of post-radiotherapy chest radiographs show reduction of volume on the treated side). Where lung function is already defective the radiation damage may be the last straw which produces a respiratory cripple. In a personal series of 68 unselected patients no less than five became permanently symptomatic (four asthmatics and one who had had a pulmonary embolism) after post-operative radiotherapy.

Radiation reduces the incidence of local recurrence and is unavoidable for many patients as the lesser evil. However, it is never without side effects and should be prescribed with judgement. Breast preservation is a poor management if the result is a permanently dyspnoeic patient, who might have avoided radiotherapy altogether, had she had a mastectomy.

Yours etc.,
ANN E. JOHNSON

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(Received 24 June 1991, accepted 23 July 1991)

References

LUND, M. B., MYHRE, K. I., MELSOM, H. & JOHANSEN, B., 1991. The effect on pulmonary function of tangential field technique in radiotherapy for carcinoma of the breast. *British Journal of Radiology, 64*, 520–523.

Authors' reply

THE EDITOR—SIR,

We thank A. E. Johnson for her interest in our paper. It is true that we only investigated patients without a history of respiratory disease or symptoms and with normal lung function. This was done not so much in fear of a critical reduction in lung function, but more out of concern that a reduced or variable lung function due to respiratory disease *per se*, would mask a radiation-induced effect. The magnitude of decrease in lung function that we found makes us believe that this approach was correct. We agree with A. E. Johnson that theoretically radiotherapy can lead to respiratory failure, but in our opinion only in patients with marginal lung function prior to such treatment.

We were surprised to learn that four asthmatics became permanently dyspnoeic after radiotherapy, especially since radiation is not a recognized modulating factor in asthma. The study referred to is, to our knowledge, not published and since A. E. Johnson's letter contains no details on pre-treatment respiratory data or the treatment itself, we are not in a position to give specific comments. Our own results and those of others still make us believe that the tangential field technique is a safe procedure in the overwhelming majority of patients receiving breast-preserving treatment.

Yours etc.,
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(Received 24 July 1991, accepted 4 September 1991)

The reduction in radiation dose for intra-oral radiographs by the use of thin K-edge filters

THE EDITOR—SIR,

The paper by MacDonald-Jankowski and Lawinski (1991) seems to infer that K-edge filters have some special property which reduces radiation dose. I would contend that the evidence they present can only justify the conclusion that the addition of filtration to the X-ray beam causes its average energy to increase and the proportion of the filtered spectrum absorbed by tissues overlying the image receptor to decrease.

For instance, if you introduce additional aluminium into the X-ray beam to equalize the aluminium spectrum to the yttrium, niobium and erbium spectra, respectively at 40 keV you would require about 3.6 mm, 4.1 mm and 5.9 mm of aluminium, respectively. The total aluminium filtration of the beams, 6.3 mm, 6.8 mm and 8.6 mm compare favourably with their measured K-edge filtrations of 6.0 mm, 7.0 mm and 9.0 mm, respectively (Table II). Similarly the more heavily aluminium filtered spectra compare favourably with those shown in Fig. 2 with the mean energy of the aluminium spectra being about 42.0, 42.3 and 43.7 keV compared with the Table I values of 42.9, 43.1 and 43.1 keV, respectively.

My calculations are based on dividing the published spectra into 10 keV portions and cannot, therefore, be presumed to be anything other than approximate. However, the similarity of the values calculated compared with those published makes one question whether the patient radiation dose is reduced by using filters incorporating K-edge filtering materials compared with more conventional, less expensive filtering materials giving beams of the same mean energy or total filtration.

Yours etc.,
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(Received 24 June 1991, accepted 23 July 1991)

References

MACDONALD-JANKOWSKI, D. S. & LAWINSKI, C. P., 1991. The reduction in radiation dose for intra-oral radiographs by the use of thin K-edge filters. *British Journal of Radiology, 64*, 524–528.

Author's reply

THE EDITOR—SIR,

In reply to the letter by R. Wilks regarding our paper (MacDonald-Jankowski & Lawinski, 1991) we would like to make the following comments.

We do not infer that K-edge filters have some special property that reduces radiation dose. In the paper it is explained that in certain materials the K-edge is at a suitable energy to shape the X-ray spectrum in such a way that the lower energy radiations are removed more effectively than by using additional thicknesses of a material with no K-edge within the required energy range (such as aluminium). It is the shape of the spectrum (in particular at lower energies) that is of more importance than the mean energy.

Additionally, one of the major reasons for investigating the particular filter systems described is that they are all commercially available products (on offer to both X-ray and dental X-ray departments) and the study enabled us to compare our finding with the claims made in the product data.

Yours etc.,

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(*Received 9 August 1991, accepted 4 September 1991*)

An innovative method for neuraxis radiotherapy using partial transmission block technique

The Editor—Sir,

I wish to comment on the paper by Plowman & Doughty (1991). The authors describe an interesting method for cranio-spinal radiation using a PTB technique. They "believe such techniques will become standard practice". However there are two potential disadvantages:

(1) The total neuraxis dose (*e.g.* 3500 cGy) is unchanged while the number of fractions is increased from the present 20–25 in 4–5 weeks to 35 in 7 weeks. This may reduce late neurological damage, but may also reduce tumour control. Reductions in effective neuraxis dose may increase the risk of relapse.

(2) The authors highlighted the increased use of chemotherapy before neuraxis radiotherapy. It is useful to begin radiotherapy after such chemotherapy with the "boost" treatment to the primary site allowing further bone marrow recovery before full neuraxis radiation. This minimizes treatment delay. This advantage is lost with the PTB technique.

Perhaps the authors would comment?

Yours etc.,

B. Magee

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(*Received 16 July 1991, accepted 4 September 1991*)

Reference

Plowman, P. N. & Doughty, D., 1991. An innovative method for neuraxis radiotherapy using partial transmission block technique. *British Journal of Radiology, 64*, 603–607.

Authors' reply

The Editor—Sir,

B. Magee raises an interesting and important issue. The radiobiological data available (Plowman, 1989; Plowman & Doughty, 1991; Steel & Wheldon, 1992) support the concept that paediatric tumours will respond to low fraction sizes. The historical data from 40 to 50 years ago where, particularly French workers, treated gliomas with low fraction sizes and our own more recent anecdotal experience of initiating similar treatment for gliomas with incipient pressure (Plowman et al, 1987), both support the concept that even gliomas will respond to low fraction size radiotherapy.

Given that late neuropsychometric morbidity is the major concern in the follow-up of cured children with the diseases for which neuraxis radiotherapy is used, given improved neoadjuvant chemotherapy (Douek et al, 1991; Sebag-Montefiore et al, 1991) and given the accumulating data against lowering the total neuraxis dose (Deutsch et al, 1991; SIOP trial unpublished data) it would seem appropriate to explore a technique that is more "CNS friendly". Our limited anecdotal experience with the technique thus far does not suggest a higher CNS relapse rate, but this is certainly under intense review.

If a boost portal is required (for example the second case illustrated in our manuscript) then this could indeed be given first if the clinician wished.

Yours etc.,

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D. Doughty

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(*Received 6 August 1991, accepted 4 September 1991*)

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Steel, G., Wheldon, T. E., 1992. Radiation biology of paediatric tumours. In: *Paediatric Oncology - Clinical Practice and Controversies*. Ed. by P. N. Plowman and C. R. Pinkerton (Chapman Hall, London).

Is the coned lateral lumbosacral junction radiograph necessary for radiological diagnosis?

The Editor—Sir,

We read with interest the article by Lipton et al (1991). A number of points are worthy of mention.

The authors do not state the centring point for the lateral lumbar view. Eisenberg et al (1979) make the comment that this can vary by up to 10 cm in relation to the iliac crest. Lipton et al (1991) indicate that the lumbosacral junction was visualized adequately in 79% of patients and if the coned view is performed in everyone, then 79% of patients will be unnecessarily exposed to additional radiation.

The policy that we have adopted following the guidelines of the NRPB, is to centre 1 cm above the iliac crest for a full length lateral view and leave it to the discretion of the radiographer to determine whether or not this has resulted in a diagnostic film of the lumber spine in the lateral projection. It is our intention to publish the results of this approach when a sufficient number are available.

Yours etc.,

G. LAMB
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(Received 31 July 1991, accepted 4 September 1991)

Reference

EISENBERG, R.L., ATKIN, J.R. & HEDGCOCK, M.W., 1979. Single, well centred lateral view of the lumbosacral spine: is a coned view necessary? *American Journal of Roentgenology, 133*, 711–713.

Authors' reply

THE EDITOR—SIR,

May we thank Lamb and Davies for their comments. We apologise for omitting the centring point for the lateral lumbar spine view. We used the lower costal margin as the departmental standard.

We certainly did not intend any implication that all patients require a coned lumbosacral junction (LSJ) view. Quite the reverse! In our study, using the grading system, we showed that it was possible to predict accurately those patients with occult pathology in this region when a LSJ view was unavailable. We concur with Lamb and Davies that, provided a radiologist or experienced radiographer assesses the lateral lumbar view at the time of examination, a coned view can be avoided in those with Grade 1 visualization (*i.e.* full visualization of the end plate of L5 and the superior end plate of S1), but should be performed in those with Grade 2 or Grade 3 visualization.

Yours etc.,

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(Received 21 August 1991, accepted 4 September 1991)

Reference

LIPTON, M. E., PELLEGRINI, V. & HARRIS, I., 1991. Is the coned lateral lumbosacral junction radiograph necessary for radiological diagnosis? *British Journal of Radiology, 64*, 420–421.

Ultrasonic detection of parathyroid adenomas

THE EDITOR - SIR,

Murchison et al (1991) are to be congratulated on the high accuracy they report for the pre-operative localization of large parathyroid tumours in a small series, and their figures confirm the supremacy of ultrasound for pre-operative localization in primary hyperparathyroidism.

With modern high-resolution ultrasound equipment, it is still impossible to demonstrate reliably normal parathyroid glands and it is difficult to detect small tumours, those located in unusual ectopic sites such as lateral to the carotid sheath and, as with frozen-section histology, distinguish adenoma from hyperplasia. All the cases they describe had a "positive" ultrasound scan and apart from the one intrathyroidal parathyroid tumour, no ectopic glands or cases of hyperplasia are described. If their series was of all patients undergoing pre-operative attempts at ultrasound parathyroid localization during the study period, the inclusion of patients with a "negative" scan might result in their figures for sensitivity and specificity approximating to other published data.

Yours, etc.,

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(Received 23 August 1991, accepted 13 September 1991)

Reference

MURCHISON, J., MCINTOSH, C., AITKEN, A. G. F., LOGIE, J. & MUNRO, A., 1991. Ultrasonic detection of parathyroid adenomas. *The British Journal of Radiology, 64*, 679–682.

Authors' reply

THE EDITOR—SIR

We thank M. Lloyd for his comments.

In our study all patients presenting with biochemical evidence of primary hyperparathyroidism and raised parathormone levels did in fact undergo pre-operative localization with ultrasound. All scans were positive. If there had been any negative scans we would have included them in our figures. We do acknowledge that had there been any ectopic parathyroid adenomas in our series then this might have resulted in a lower sensitivity.

Yours, etc,

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1992, *The British Journal of Radiology*, 65, 96–99

Proceedings of the British Institute of Radiology

Ultrasonic assessment of bone

Abstracts of papers presented at a one day symposium organized by Sheffield City Polytechnic in conjunction with National Osteoporosis Society, held at the Royal Victoria Hotel, Victoria Station Road, Sheffield on Wednesday 29 May 1991

Ultrasonic measurement techniques, by C. M. Langton
Relationships between ultrasonic and material properties, by G. P. Evans
Propagation of ultrasound in cancellous bone, by R. X. Boutinaud
Bone ultrasound from the bottom up, by J. A. Evans
Comparison of ultrasound with DEXA, by R. Eastell, K. E. Naylor, A. Abdulrahmen, T. W. D. Smith and C. M. Langton
Screening for osteopenia: a comparison between BUA and DXA, by R. J. M. Herd, G. M. Blake, J. C. Parker and I. Fogelman
BUA precision and age related dependence, by J. G. Truscott
Population Studies, by D. W. Purdie

Screening for osteopenia: a comparison between BUA and DXA, by R. J. M. Herd, G. M. Blake, J. C. Parker and I. Fogelman
BUA precision and age related dependence, by J. G. Truscott
Population Studies, by D. W. Purdie

Ultrasonic measurement techniques

C. M. Langton
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Tissue characterisation of bone. Conventional industrial non-destructive testing (NDT) and medical applications of ultrasound tend to use frequencies in the range 2.5–10 MHz. Owing to the highly attenuating nature of cancellous bone, frequencies less than 1 MHz have to be used, adopting a transmission technique where one transducer acts as transmitter and a second acts as receiver. Osteoporosis may be defined as a change in density and structure predominantly of cancellous bone leading to a reduction in skeletal integrity and hence an increased risk of fracture. We may use ultrasound to characterize the physical properties of a material such as cancellous bone, measuring either the velocity or attenuation. Velocity is calculated by dividing the thickness of a sample by the transit time for an ultrasonic pulse through it. A measurement of bone velocity as opposed to limb velocity may be obtained by correcting for overlying soft-tissue. Broadband ultrasonic attenuation (BUA) describes the increase in ultrasound attenuation over a particular frequency range, typically 0.2–0.6 MHz. *Bone measurement systems.* The first commercial prototype system developed to measure BUA in the calcaneum incorporated a water bath containing two ultrasonic transducers maintained at a fixed separation, the transmitting transducer being connected to a computer interfaced variable frequency tone-burst generator. The development of this technique has been pursued by Walker Sonix Inc. WALKER SONIX UBA 575. Developments to the initial design include improved water handling, incorporation of a recti-linear scanning system and a pneumatic foot restraint to improve measurement reproducibility. ACHILLES. The LUNAR ultrasound densitometer provides both speed of sound (velocity) and BUA. The densitometer features automated water handling, with storage tanks incorporated in the instrument. CUBA. The contact ultrasonic bone analyser (CUBA) was developed initially for the measurement of the thoroughbred racehorse in training, where rapid data collection and removal of the water bath were deemed essential. CUBA provides both BUA and velocity information for cortical and cancellous bone; an important feature being the correction of overlying soft-tissue to provide an accurate measurement of bone velocity.

Relationships between ultrasonic and material properties

G. P. Evans
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The successful prediction of fracture risk requires a multifactorial approach. From a mechanical perspective both structural and material factors are implicated in the failure process. The velocity of sound in a material is related to the Young's modulus of elasticity and the density of the material. Since both velocity and modulus are determined to some degree by the nature of the interatomic bonds in the material, this relationship is predictable. While the theoretical strength of a material is also a consequence of the strength of the interatomic bonds, in practice failure initiates at a flaw in the material There is, therefore, no relationship between strength and ultrasound velocity. The relationship between velocity and modulus, and between velocity and density have been shown to yield strong correlations in both cortical and cancellous bone. The relationship between material properties and density for cancellous bone has been extensively researched. The density of such a cancellous material is an important property in determining its behaviour under load, and a variety of techniques such as SPA and DEXA have been developed to measure density *in vivo* as an indicator of fracture risk. The relationship between density and material properties in cellular materials, however, is complicated by the cell structure or architecture. At low densities the individual trabeculae are rod-like in appearance, while at higher densities a more plate-like structure is apparent. The orientation of the trabeculae as well as the degree of connectivity between them are also important considerations. The importance of trabecular architecture in determining the properties of cancellous bone suggests that methods that take account of architecture, as well as density, will prove to be better predictors of material properties (and ultimately fracture risk) then those that do not. Broadband ultrasound attenuation (BUA) has been shown to be related to architecture and density, and is therefore a potentially better indicator of the mechanical competence of cancellous bone than ultrasound velocity.

Propagation of ultrasound in cancellous bone

R. X. Boutinaud
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Our current research aims to quantify the propagation of ultrasound through cancellous bone and transpose the ultrasonic parameters of velocity and attenuation into material parameters such as density, elasticity, structure, etc. To achieve such a task we intend to use the Biot theory. This theory analyses the separate motion of the porous structure (mineralized trabecular framework) and the interspaced fluid (bone marrow) induced by the ultrasonic wave. This approach considers the energy loss due to the frictional interaction of the marrow flowing within a trabecular framework cell, and the inelasticity of the trabecular bone framework. There are 11 physical parameters required for the Biot theory concept: the porosity of cancellous bone; the density and viscosity of the marrow; density of mineral bone; the permeability of the trabecular framework; the bulk modulus of the marrow and mineral bone; the rod velocity and the shear velocity of the trabecular framework; the logarithmic decrement for longitudinal and shear vibration of the frame. The last four parameters evaluate the elasticity of the frame. In addition to these, two other parameters are needed to describe the shape and orientation of the trabecular framework cells. Unfortunately, they cannot be defined theoretically but have to be obtained from experimental investigation. In order to establish and relate these parameters to known physical parameters, we have used a perspex cube as a bone phantom. To mimic a simplified, but well defined trabecular framework, we have drilled holes of a certain diameter into the cube. A visco-elastic bone marrow mimic such as castor oil may then be placed into the holes. A computer program has been developed based on the Biot theory, incorporating the geometrical parameters as fitting values. Comparing the theoretical predictions with experimental measurements of BUA will enable us to validate the Biot theory.

Bone ultrasound from the bottom up

J. A. Evans
Department of Medical Physics, University of Leeds, Leeds General Infirmary, Leeds LS1 3EX

Attenuation and velocity measurements made on the constituent materials of intact bone are compared with values obtained from its main constituent materials, fat, collagen and hydroxyapatite. Measurements on the bone samples and fat were made at 1 MHz in a water filled perspex tank, while measurements on the HAP were made with a different apparatus in which two perspex buffer rods are held together under pressure to establish acoustic contact with the samples. Both velocity and attenuation were measured short acoustic pulses. The received signals were digitized and stored prior to Fourier analysis. For the tank experiments, the amplitudes computed as a function of frequency were corrected by subtracting the corresponding values obtained from a reference trace obtained with only water present. Corrections were made for the reflections at the various interfaces present. Sample densities were measured using an Archimedes principle technique. The attenuation values obtained for fat, collagen and HAP were 0.58, 0.65 and 2.50 dB/cm/MHz, respectively, which would lead to a predicted attenuation of 1.18 dB/cm for intact bone in the absence of scattering losses. The bone samples had attenuation values of 20–30 dB and 2.5–3.0 dB/cm/MHz for cancellous and cortical bone, respectively. Hence, it was concluded that scattering is the dominant loss mechanism at these frequencies. The samples were then attacked with nitric acid which removed the mineral component and therefore caused the density to fall. The correlation between the density values at each stage of demineralization and the attenuation was in the range 0.68–0.97, whereas the velocity correlation with density was much better at 0.99. Similar results were obtained when the density of all the samples before demineralization was compared with the velocity and attenuation. It was concluded that the contribution of scatter to the total attenuation is significant in all cases but is much greater for cancellous than cortical bone. For cancellous bone at 1 MHz, the scattering contribution to the total attenuation is almost an order of magnitude greater than the absorption contribution. It can be assumed that the scatter contribution is primarily due to the trabecular structure in the bone. The velocity of ultrasound in both cancellous and cortical bone depends almost entirely upon density. Therefore, this will correlate well with X- and γ-ray measurements, but cannot be expected to predict bone strength reliably.

Comparison of ultrasound with DEXA

R. Eastell, K. E. Naylor, A. Abdulrahmen, T. W. D. Smith and C. M. Langton
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Dual-energy X-ray absorptiometry (DEXA) is an accurate and reproducible technique that may be used to measure bone mineral content of skeletal sites that commonly fracture in osteoporosis (hip, spine). Broadband ultrasound attenuation (BUA) has been compared with DEXA in groups of normal women and women with vertebral fracture. Although four studies have reported significant correlations between DEXA (spine or hip) and BUA (calcaneus) of between 0.4 and 0.8 (correlation coefficients), the relationship was not strong enough to allow accurate prediction of DEXA from BUA. However, BUA reflects bone architecture and so may provide information about fracture risk that is not available by DEXA. To evaluate this, the diagnostic sensitivity and specificity have been compared for vertebral fracture in four studies. BUA and DEXA were reported to have similar diagnostic accuracy. BUA may be able to predict fracture risk as well as DEXA. The best way to evaluate this is to measure a cohort of women with BUA and DEXA and evaluate fracture rates prospectively. Such studies are currently in progress.

Screening for osteopenia: a comparison between BUA and DXA

R. J. M. Herd, G. M. Blake, J. C. Parker and I. Fogelman
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We report a study comparing measurements of broadband ultrasonic attenuation (BUA) in the calaneus performed with a

Walker-Sonix UBA-575 with dual energy X-ray absorptiometry (DXA) scans of the lumbar spine and femoral neck obtained with a Hologic QDR-1000. The study included 121 women (mean age 53.0) referred for perimenopausal screening for osteopenia. A further 29 women (mean age 65.6) with osteoporotic vertebral fractures were also studied. Duplicate BUA measurements in one heal in 30 patients gave a coefficient of variation of 4.6%. BUA measurements in both heels in 90 patients showed a high correlation between right and left ($r = 0.89$) with no systematic difference between the two sides (right–left = $+0.9 \pm 1.0$ (1 SEM) dB/MHz). After exclusion of patients with factors predisposing to low bone density, the screening group was used to define the normal range for BUA as a function of age. Linear regression analysis gave the following relationship: $\text{BUA} = 90.3 - 0.85\,(\text{Age} - 40)$ dB/MHz (SEE = 13.3 dB/MHz). ROC analysis was used to examine the comparative ability of BUA and DXA measurements to differentiate between patients in the screening and osteoporotic fracture groups. The areas under the three ROC curves were virtually identical (BUA: 0.83; lumbar spine BMD: 0.83; femoral neck BMD: 0.84) showing that BUA was as effective as axial BMD in distinguishing patients in the two groups. Scatter plots and ROC analysis were used to investigate the ability of BUA measurements to identify screening patients with osteopenia. For this purpose osteopenia was defined as an axial BMD value below the 30th centile of an age matched normal population. The results showed that BUA was poor at predicting axial BMD (BUA *vs.* lumbar spine BMD: $r = 0.62$; specificity = 46% at a sensitivity of 80%; area under ROC curve = 0.44; BUA *vs.* femoral neck BMD: $r = 0.53$; specificity = 42% at a sensitivity of 80%; area under ROC curve = 0.32). *Conclusions.* The ability of a BUA measurement to identify osteopenia in a perimenopausal screening population was poor. However, the ultrasonic technique was as sensitive as DXA in differentiating between patients with osteoporotic spinal fractures and patients in the screening group.

BUA precision and age related dependence

J. G. Truscott

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Dual energy X-ray absorptiometry (DEXA) of the spine, femur and total body (Lunar DPX), single photon absorptiometry (SPA) of the forearm (ND1100A) and broadband ultrasonic attenuation (BUA) of the heel (UBA1001, UBA575) were compared. For the UBA1001 *in vitro* over 13 months the reproducibility was 3.1% and *in vivo* over the same period 9.6%. Before measuring reproducibility of the UBA575 we had to find a suitable wetting agent. A 2% solution of Stardrops proved to be the best of those tested. Talcum powder and body lotion have an effect on reproducibility and pre-bathing the foot in soapy water followed by an alcohol swab of the heel helps. For the UBA575 *in vitro* over 3 months reproducibility was 2.2%. *In vivo* reproducibility over 5 days was 2.8%, over 10 min it was 3.5% and over 3 months it was 6.6%. This improvement is attributable to a change in the transducers, a change to rectilinear scanning and a foot restraint. Comparing BUA with DEXA and SPA yields the following correlations (r, p): UBA1001 spine (0.34, < 0.001), femur (0.27, < 0.01), total body (0.31, < 0.02) and distal forearm (0.29, < 0.01) and UBA575 spine (0.61, < 0.001), femur (0.60, < 0.001), total body (0.54, < 0.001) and distal forearm (0.55, < 0.001). This improvement is due to the improvement in precision. Reasons for poor correlation could be that BUA reflects both density and structure of bone, and correlation between bone density at different sites may not be good. The relationship of BUA with age is similar to that of DEXA of spine and femur in the same subjects. Future work on ultrasound techniques should include the development of normal ranges of BUA against age, the assessment of the relationship of BUA to fracture incidence to define an indicator of fracture risk and the determination of the effects of scatter and its relationship to the structure and strength of bone.

Population studies

D. W. Purdie

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The condition of osteoporosis is one of high prevalence in Western societies and is responsible for a rising incidence of osteoporosis-related fracture of spine and femoral neck. The current cost to the NHS is unknown, but is probably not less than £500 m per annum. Treatment of the established disease is unsatisfactory and is unlikely to improve in the short or medium term. Given that prevention of bone loss with oestrogen, diphosphonates or calcitonin has been clearly shown and that the former appears to reduce the incidence of fracture, the next step is to enquire if it is possible to identify the population at risk at a time when primary prevention may be offered. The means available for potential screening of populations are; historical—through indentification and weighting of risk factors; biochemical—through identification of individuals losing bone rapidly, and; biophysical—through identification of individuals with a low bone mass anterior to fracture. Studies have so far failed to demonstrate that osteoporosis risk factors, which are valid for populations, are applicable to individuals. Equally, biochemical screening is not, so far, suitable for population studies because of the dietary preparation and fasting required before the plasma and urine analyses. Biophysical testing, however, which is non-invasive and requires no preparation, is eminently suitable for mass studies, provided that the technique is precise, accurate and capable of handling large numbers of patients. We have utilized DEXA in a study of the viability of primary screening in 50–54 year old women in the Yorkshire cities of Kingston upon Hull and Beverley. (Population of 500 000.) The protocol calls for skeletally protective regimes of HRT to be offered to all women in the cohert whose BMD values fall at or below the 25th centile for the normal population. The 25th centile values for our population at L2–L4 and femoral neck are 1.043 g/cm^2 and 0.845 g/cm^2, respectively. To date 4000 patients have been studied, the centile values for the population have been established and the acceptability of the process to the public and primary care sectors has been tested. Data from the first 1000 patients screened will be presented and discussed.

Screening for osteoporosis: comparison of dual energy X-ray absorptiometry (DXA) and broadband ultrasound attenuation (BUA)

D. M. Reid

Osteoporosis Screening Unit, City Hospital, Aberdeen

Introduction. Post-menopausal osteoporosis may be identifiable in the pre-symptomatic phase by measurement of bone density. BUA of the os calcis, when used in combination with a low cognisance score, will successfully predict hip fractures in a

	BUA	L 2-4	Neck	Troch	Wards
BUA	—	r = 0.269	r = 0.187	r = 0.257	r = 0.186
L 2-4		—	r = 0.587	r = 0.594	r = 0.541
Neck			—	r = 0.688	r = 0.805
Troch				—	r = 0.650

(All correlations significant at the $p < 0.0001$ level.)

population of elderly women. To test the feasibility and practicality of a population based programme based on DXA of the axial skeleton, an osteoporosis screening unit has been opened in Aberdeen. This report examines the initial comparison of DXA measurements of hip and spine bone density with BUA measurements of the os calcis in detecting those at risk of osteoporosis. *Methods.* Women aged 45–49 are identified randomly from a population based health register. A single measurement of hip and lumbar spine DXA and BUA of the os calcis is carried out. *Results.* To date 466 women with a mean age of 46.9 years have undergone both DXA measurements of hip and spine and BUA measurements of the os calcis. Correlations between BUA and the 4 DXA measurement sites are shown in the Table above.

Discussion. BUA measurements are significantly correlated with DXA measurements of the spine and hip, but the correlation coefficients are numerically weak. Analysis of quartiles shows that if BUA were to be used as a pre-screening device to determine those women who have a DXA measurement in the lowest quartile and if one were to use a BUA below the mean as an indicator, the sensitivity of such an approach would be only 66% and the specificity 54%. These results strongly suggest that BUA can not be used to predict accurately those women with a slow spine and hip BMD. It remains to be seen whether BUA or DXA will be shown to be better predictors of future risk of hip or spine fractures.

Broadband ultrasonic attenuation in active and sedentary men and women

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These studies examine the potential of broadband ultrasonic attenuation (BUA) in the calcaneus to discern (a) differences in bone quality between groups of individuals differing in their physical activity levels, and (b) changes resulting from regular exercise. Two groups of males aged 16–26 years, one physically active and one sedentary, were compared. Active individuals engaged in at least 6 hours per week of weight-bearing exercise whilst sedentary subjects took less than 1 hour per fortnight. Both BUA (Osteosonics), the attenuation for a cylindrical sample of bone of known cross-sectional area, and BUA normalized for bone width were higher in active than sedentary men (159.2±4.3 cf 128.6±3.6 dB MHz^{-1}, $p < 0.05$; 43.7±1.06 cf 35.1±1.06 dB MHz^{-1} cm^{-1}, $p < 0.05$, respectively) (Mean±SEM). Our second study examined the influence of brisk walking on BUA (Osteosonics) in formerly sedentary women aged 30–61 years (25 walkers, 15 controls). Walkers completed 159±46 mins per week of brisk walking at a speed of 1.72±0.05 ms^{-1}, *i.e.* about 16–18 km^{-1} per week. After 1 year BUA values were increased ($p < 0.05$) for walkers relative to controls (walkers 103.3±4.9 *vs.* 116.1±3.8 dB MHz^{-1}; controls 103.6±5.5 *vs.* 99.6±5.4 dB MHz^{-1}).

Finally, BUA (Walker Sonix UBA 575) was compared in young adult females aged 18–22 years differing in habitual physical activity level. 48 females were classified by hours of exercise per week, *i.e.* < 2 h, 3–5 h and > 5 h. Mean BUA values were 97.6±3.1 dB MHz^{-1} for the lowest activity group ($n = 14$), 105.4±2.8 dB MHz^{-1} for the middle group ($n = 22$) and 111.0±1.9 dB MHz^{-1} for the high activity group ($n = 12$). Values for the high activity group were greater ($p < 0.05$) than those for the lowest activity group. Thus, in cross-sectional and longitudinal studies, BUA reveals differences in bone condition in the calcaneus which reflects habitual physical activity levels.

Prediction of fracture risk in the racehorse

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Fractures in the horse racing industry are a cause of considerable wastage. It has been found that of 125 fracture cases studied at racecourses, 21 were of a spontaneous nature. Spontaneous fractures occur unexpectedly when the horse is travelling at speed during flat racing or between fences. The fracture appears to be atraumatically induced and generally affects bones of the distal forelimb. There are no clinical signs of lameness prior to fracture. It has been shown that the mechanical competence of certain bones may be incompatible with the stresses applied to them at certain *in vivo* strain rates and that certain bones are predisposed to spontaneous fracture, *i.e.* these bones are suffering from a material insufficiency. An ultrasound system, the contact ultrasound bone analyser (CUBA) is being used to scan large numbers of thoroughbreds in racing and training. CUBA is capable of measuring ultrasound velocity and broadband ultrasound attenuation (BUA) through the third metacarpal bone (a bone, commonly the site of spontaneous fractures). Should the different material properties of the susceptible bone be demonstrated in the ultrasonic parameters measured, then there is a means of identifying the horse at risk of fracture. The study involves: (a) screening a large cross section of horses in training to determine normative data; (b) a longitudinal study of horses entering training as 1 year olds and making monthly measurements during their development, and (c) a comparison of ultrasound measurements to mechanical and microstructural properties implicated in spontaneous fractures. Results to date have demonstrated that transmission ultrasound velocity increases with an increase in skeletal maturity, as was predicted. The results for BUA require further study before conclusions can be made, but it would appear that BUA measurements are very sensitive to structural changes within the developing skeleton.

1992, *The British Journal of Radiology*, 65, 100

Book reviews

Gastrointestinal Cancer: Radiation Therapy. Ed. by R. Dobelbower, pp. xiv + 301, 1990 (Springer Verlag, Berlin), DM 220.
ISBN 3-540-50505-9

This book aims to provide an update on the subject of the management of patients with gastrointestinal malignancies, particularly by radiotherapy but details of chemotherapy are also given where appropriate. The volume is a multi-author book, each chapter being devoted to the treatment of one specific tumour type. All the authors are North American; indeed all are from the United States with one notable exception. As a result, the book has a quite distinct North American flavour.

It is difficult to know who will benefit from reading this particular volume. Each chapter is set out using the same format in which the anatomy, natural history, epidemiology, pathology and staging are first described. The general principles of treatment are then discussed and there is a summary of surgical management prior to embarking on the main meat of the chapter, which is the radiotherapy and chemotherapy aspects of treatment. This makes the book very repetitious. In addition, there is, only naturally, a brief resumé of topics such as the anatomy and natural history of the disease and therefore it is of very limited use in this respect. The majority of readers who would wish to obtain details of these aspects of the disease would find much more useful information elsewhere.

It is particularly disappointing in some chapters that key European references are totally ignored. Indeed the emphasis throughout the book is towards North America and this limits its general usefulness. Another major criticism of the book is that although each chapter reviews, in great detail, published work on radiotherapy and chemotherapy for each tumour type, there is little attempt to draw any conclusions from the literature and state what the authors consider is the most appropriate course of action to take in any individual case. The fact that some major multicentre European trials are being carried out for some of the tumours under consideration, e.g. anal cancer, is similarly not mentioned.

The majority of individuals would not wish to buy this expensive book but will prefer to use the library copy for reference.

S. J. Arnott

Methods of Hyperthermia Control. Ed. by M. Gautherie, pp. ix + 130, 1990 (Springer-Verlag, Berlin), DM 156.
ISBN 3-540-50978-X

This expensive, slim volume is divided into three distinct chapters. Part I "Thermometry in therapeutic hyperthermia" reviews the current methods of invasive thermometry used in the clinic. This chapter adequately describes methods of probe implantation for both superficial and deep hyperthermia together with a review of available technologies for invasive thermometry with their respective measurement errors and artefacts.

Part II "Non-invasive control of hyperthermia" takes up nearly half the book in reviewing the exciting research into non-invasive methods of temperature measurement in tissue. The authors describe in detail the many techniques that have been considered for deep thermal imaging, although only a few of these methods have approached the necessary performance requirements for non-invasive thermometry in clinical hyperthermia. Finally, Part III "Temperature measurement by microwave radiometry" describes the development and implementation of a radiometric controlled microwave hyperthermia system from France (University of Lille). The author presents the methods employed to predict thermal profiles in tissue from microwave radiometric measurements and the bio heat equation using an inverse data process.

In general, the book has excellent aims but leaves the reader with the overall impression that the subject of 'hyperthermia control' is in its infancy and may never achieve the goal of total non-invasive treatment. A great deal of repetition is evident throughout the book, particularly on the subject of microwave radiometry, the principles of which are described in chapters two and three. The presentation of the reference list at the end of each section changes from chronological to alphabetical, this could have been standardized by the editor. The layout of the book is of a very high standard, although differences of style are obvious and inevitable from a multi-author work. A few colour illustrations have been included where the authors feel this is appropriate.

This book probably provides a good up-to-date picture of progress in this specialized area of hyperthermia research. However, I would not recommend this as being appropriate for purchase by a small library. Those individuals who are embarking on research in medical thermometry, particularly the non-invasive type, should consider this book as essential reading. Owing to the high cost of this book, many readers will inevitably borrow from a large lending library or purchase a book that gives a comprehensive account of hyperthermia techniques for the same price. In conclusion, I feel that this book summarizes the past 10 years, research in hyperthermic thermometry well, with the authors' plea for continued support for their and others' work in this field. The book will appeal to a small readership but nevertheless fills a subject gap in the clinical thermology subseries on thermotherapy.

J. Conway

1992, *The British Journal of Radiology*, *65*, 101–102

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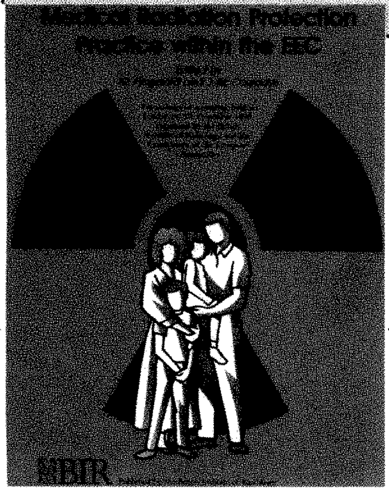
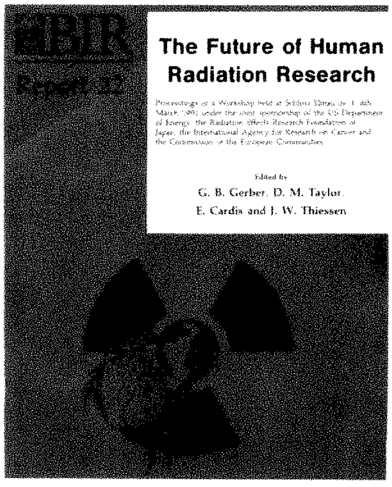
The BIR is delighted to announce that it has just published three new books. Full details and order forms can be obtained from the BIR Publications Department. Remember, all BIR members receive a 25% discount on BIR publications. We are always pleased to receive your comments on our publications, and other proposals for new projects.



Medical Radiation Protection Practice within the EEC

Proceedings of a meeting held in London on 5th December 1990, organized by the **BIR** and the **CEC.**

- 11 papers by experts from six countries directly involved in the formulation and implemention of Directives.
- Overview of European Safety Legislation and the impact of harmonization.
- Implemention of directives affecting the general public, healthcare workers and patients.
- Calibration requirements for radiation dosemeters
- Review of scientific basis for standardization in radiology.
- This publication will be of interest to everyone concerned with radiation protection.


BIR
Report 22
The Future of Human Radiation Research
Edited by
G. B. Gerber, D. M. Taylor,
E. Cardis and J. W. Thiessen

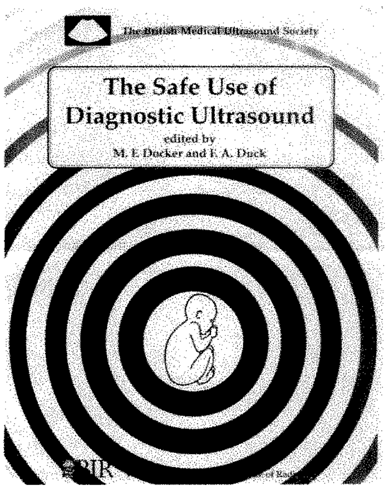
The Future of Human Radiation Research

Contains the full review papers presented at a workshop held at Schloss Elmau on 4th-8th March 1991 under the joint sponsorship of the US Department of Energy, the Radiation Effects Research Foundation of Japan, the International Agency for Research of Cancer and the Commission of the European Communities.

The Safe Use of Diagnostic Ultrasound

From BMUS and the BIR, a practical reference for everyone working in ultrasound, *The Safe Use of Diagnostic Ultrasound* explains how to operate diagnostic ultrasound equipment to minimize any risk of hazard to patients.

The internationally respected contributors believe that this publication will be invaluable to everyone working with diagnostic ultrasound.


The British Medical Ultrasound Society
The Safe Use of Diagnostic Ultrasound
edited by
M. E. Docker and F. A. Duck
BIR

BIR Company Subscriber Scheme

Company Profiles — *Premise Engineering*

Established for over 35 years, Premise Engineering specialises in the design, manufacture and installation of a wide range of radiation shielding materials and equipment for hospitals and industry throught the UK and many other parts of the world. A small company, with most shielding designed and built to individual customer requirements, Premise is justifiably proud of its high standard of craftmanship.

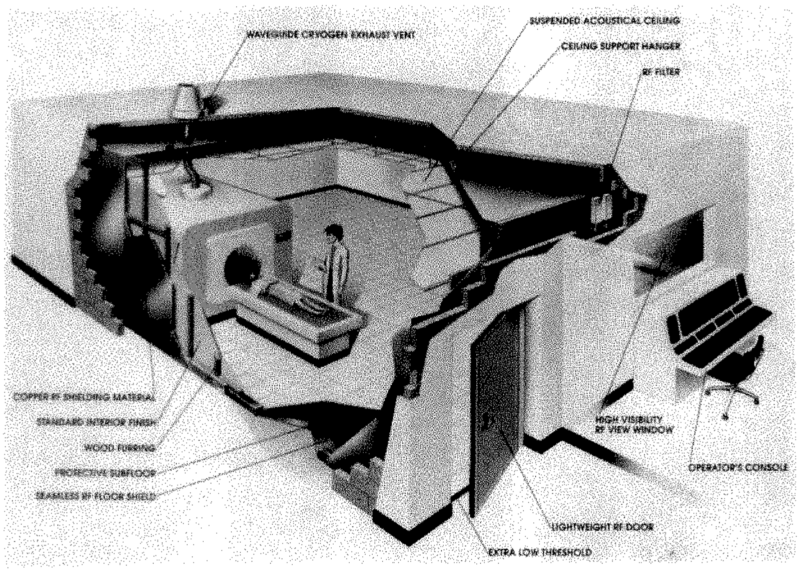
Today Premise Engineering is well-known for its lead-lined radiation protection products which include PREMPLY lead-ply panelling, lead-lined doors, screens, cabinets and windows up to the construction of complete X-Ray rooms and laboratories. A wide range of accessories is also available - apron rails and hangers, dark-room benches, cassette hatches etc. Amongst the company's latest innovations are PREMAC and PREMADEX. PREMAC, a transparent radiation protective acrylic sheet, is a product unique to Premise Engineering and has gained wide acceptance in the medical field. PREMADEX was developed in conjunction with the NRPB, Harwell and is a suitable shield wherever neutrons are found, typically in accelerator facilities, neutron source containers, gloveboxes, nuclear reactors etc.

Over the last 4 years, the company has successfully extended its range of products to include RF shielding for MRI units, utilising the Lindgren RF enclosure system under agreement with Lindgren's European representative, Imedco AG, Switzerland. This system was specifically designed for medical applications and uses copper for the RF shielding, the preferred system for all MRI manufacturers. Where sheilding is also required to contain the magnetic field steel plates can be combined with the copper for a fully integrated system.

Premise Engineering considers the users to be the most important element in the design of an RF examination room, which must be functional to use and at the same time a pleasant place to work. As a result, a number of special technical and finishing features have been developed which allow the architect to design an examination room to suit the requirements of the hospital.

Continuing its development programme, Premise Engineering is moving into the field of Teleradiology - a radiological communication system called TelePacs. This is versatile, high-resolution modular system designed to transmit all modalities of diagnostic images over standard telephone lines. Its outstanding image quality is achieved through the use of a laser film digitizer, a direct capture link to a CT or MR scanner and a radiological quality display. To facilitate and speed up diagnosis, images can be transferred rapidly from one location to another by networking hospitals, physicians, radiologists and speciality centres.

Premise Engineering is dedicated to remaining ahead of the shielding market to provide patients and radiography staff with a safe and friendly environment as they work with tomorrow's technology.



Typical MRI room

Wolters Kluwer US Corporation

Gower Medical Publishing, Raven Press and J.B. Lippincott Company represent the medical division of Wolters Kluwer U.S. Corporation.

Gower Medical Publishing publishes colour illustrated textbooks, atlases and teaching slide atlases.

Raven Press publishes health care and scientific products, especially books and journals in medicine and life sciences.

J.B. Lippincott Company publishes health care and scientific products, delivered in a wide variety of services; books, journals, CD-ROM, videos, newsletters.

Amersham International

Amersham International is a leading speciality biochemical, healthcare and quality assurance company which provides reliable, innovative products and services to customers in the life science, medical and industrial communities around the world.

Amersham International is committed to enhancing the quality of human life in striving to provide customer benefits from both its radioactive and non-radioactive technologies:

Life Science

Assays for the detection and measurement of the key components of living cells and improved understanding of biological processes and disease states

Healthcare

In vivo diagnosis of human physiological disorders cancer diagnosis and treatment

Industry

Industrial sterilisation, non-destructive testing and detection instrument calibration.

K. C. Clark Radiographic Slide Library - for teaching purposes at all levels.

In October 1991 the original K C Clark collection of slides was reassembled, catalogued and added to the wealth of books and journals already kept in The Bernard Sunley Library, which is part of the British Radiological Library Scheme.

The slide collection represents the lectures prepared at Ilford Ltd, during the years 1935 to 1980 and was also used to compile and revise the well known book *Positioning in Radiography* written by K. C. Clark.

Consisting of some 5000 3 x 3 slides, the collection includes a substantial section demonstrating normal radiographic appearances, together with many abnormal findings due to pathology or trauma. Vascular and contrast media techniques, as well as a large section on equipment, physics and geometric principles underlying the formation of the image, are particularly well presented, mostly in line diagrams. Other sections include the following subject headings: dental, veterinary, flora and fauna, industrial, and radiotherapy.

The slides may be viewed at 36 Portland Place (an approriate viewer is available, together with copies of the book *Positioning in Radiography* to provide explanatory text, diagrams and radiographs). Anyone wishing to take the opportunity to visit the slide library is most welcome to do so. Please call in at the BIR during the working hours noted below, or contact Stephen Johnson, Systems Librarian, who can also arrange for photocopy or 35 mm duplicates (at cost plus 10% adminstrative charge).

An acknowledgement of the library collection as a source noted in any subsequent publications or teaching materials will be much appreciated.

Opening hours are 9am—5pm Monday, Wednesday, Friday and 9am—7pm Tuesday and Thursday.

Contact the System Librarian, Stephen Johnson, at The Britiish Institute of Radiology, 36 Portland Place, London W1N 4AT. Tel: 071-580 4085.

New BIR Members

MEDICAL

Dr Rajiv K. **AGRAWAL**, MBBS, DMRT, MD, FRCR (Newcastle upon Tyne), Radiotherapist/Oncologist

Dr Beatrice **BEULAH**, MBBS, DMR(D), FRCR (New Zealand), Diagnostic Radiologist

Dr Richard J. C. **DUNHAM**, MB ChB, FRCR (Leeds), Diagnostic Radiologist

Dr **GRACE** GOH, MB, ChB, MRCP, DMRD (Liverpool), Diagnostic Radiologist

Dr Paul G. **PRATT**, MB, ChB, LRCP, LRCS, LRCPLS, MRCP, (London), Diagnostic Radiologist

Dr Hartmut **REINER**, (West Germany)

Dr Catherine J. **WETTON**, MB, BS, FRCS,(Manchester), Diagnostic Radiologist

Dr Aytekin **BESIM**, MB, Radiologist, of Radiology, (Turkey), Diagnostic Radiologist

Dr John S. F. **CANAVAN**, MB chB, MRCP, DMRD, FRCR (Kent), Diagnostic X-ray

Dr Rui Jorge Cunha Machado **AGUIAR**, LMS (Portugal), Diagnostic Radiologist

Dr Walter **CURATI-ALASONATTI**, MD, PhD (London), Diagnostic Radiologist

Dr Janine M. **DOMJAN**, MBBS (hons), MRCP (Kent), Diagnostic Radiologist

Dr Mark **GAZE**, MBBS, MRCP(UK), FRCR, DMRT (Glasgow), Radiotherapist/Oncologist

Dr Christine **HERON**, MRCP, FRCR (London), Diagnostic Radiologist

Dr Bleddyn **JONES**, MA, MSc, MB, Bchir, MRCP(UK) FRCR (Merseyside) Radiotherapist/Oncologist

Dr Garrett **MCGANN**, MBchB, FRCS Ed. FRCR (London), Diagnostic Radiologist

Dr Geoffrey P. **NAISBY**, MBBS, FRCS FRCR (Cleveland), Diagnostic Radiologist

Dr D Filipkumar A. **PRADHAN**, MD, DMRE (Bombay) (Tanzania), Diagnostic Radiologist

Dr Bertec **SUNDSTRUP**, MBBS, FRACR, FRCR (Australia), Radiotherapy/Oncology

Dr William D. **THOMPSON**, MBBS, MRCP (UK) FRCR (Cleveland), Diagnostic Radiologist

Dr Fei Ling **THOO**, MBBS, PART I FRCR (Singapore), Diagnostic Radiologist

NON-MEDICAL

Dr Cumali **ATKOLUN**, (London), Nuclear Medicine Specialist

Mr Richard **BOVILL**, (Taunton, Somerset), Physicist

Mr Dennis J. D.[illegible]**AGHILL**, (CEI) IEE-IENG, M[illegible]F.(W Midlands)Engineering MFR

Dr Malcolm **DAVISON**, MA, DPhil, CPhys, FInstP (Glasgow) Physicist

Mr Geoffrey **FAULKNER**, BSc, Elec. Engineering (Swindon), Executive

Dr David G. **HIRST**, BSc, PhD (Middlesex), Radiobiologist/Biologist

Mr Peter **HOGG**, DCR (R), DRI, Cap, CertCI, FER (London), Radiographer

Dr Peter N. **LONGTHORNE**, MB, BS, MRCS, LRCP, DObst, RCOG, MFPM (W Sussex), Executive

Mr Niall C. **MONAGHAN**, H-TEC, (Surrey), Nuclear Medicine Technologist

Mr Andrew J. **SCALLY**, DRC (R), BSc (Surrey), Physicist

Mr Leslie **THOMAS,** Managing Director (Glasgow), Executive

Mr Scott **BOWMAN**, DCR, HDCR, TDCR, FAETC, MA, (London), Pharmacologist/Pharmacist

Dr Malcolm **DAVISON**, MA, D.Phil, CPhys F InstP(Glasgow) Physicist

Prof Kieran P. **MAHER**, MSc (Australia) Radiobiologist/Biologist

Mr Andrew **RENNISON**, DCRR, BSc (Hons) (Lancashire), Pharmacologist/Pharmacist

Mr Patrick **REVELL**, DCR (Sussex), Radiographer

Mr Steven A. **YOUNG**, BSc, MSc (Edmonton), Radiotherapy/Oncology

Some suggestions for a reading list in the history of radiology

Jean M. Guy, Yeovil District Hospital

I have had several enquiries asking for the identity of the books mentioned in my brief article in the February 1991 issue of the Bulletin. As these were a very small sample of the literature on the subject, I have amplified this list to provide a more comprehensive source of secondary texts on the history of radiology. Not all of these books are still in print. Nothing can replace the study of the original books, journals and documents which are well represented in the historical collection of the British Institute of Radiology. General medical textbooks, medical, photographic and scientific journals and the archives of individual hospitals are important sources of information on radiological history, particularly for the years prior to 1914.

Richard F. Mould, A History of X-Rays and Radium, with a chapter on Radiation Units 1895-1937, published by IPC Building and Contract Journals Ltd., Surrey House, Throwley Way, Sutton, SM1 4QQ, 1980. ISBN 0 617 00355 6.

E. H. Burrows, Pioneers and Early Years, a history of British Radiology, Colophone Ltd, 39 Victoria St, St Anne's, Alderney, Channel Islands, Great Britain, 1984. ISBN 0 9511676 O X.

Guy Pallardy, Marie-Jose Pallardy et August Wackenheim, Histoire Illustree de la Radiologie, les editions Roger Dacosta, 19, Boulevard Raspail, 75007 Paris,1989.ISBN2 8512 074 0.

Juan A. del Regato, Radiological Physicists, published by the American Institute of Physics (335 East 45 Street, New York, New York 10017) for the American Association of Physicists in Medicine, 1985, ISBN 0 88318 469 9.

Steve Webb, From the Watching of Shadows: the origins of radiological tomography, publ Adam Hilger, Bristol and New York (IOP Publishing Ltd., Techno House, Radcliffe Way, Bristol, BS1 6NX) 1990, ISBN 0 85274 305 X.

J. A. Veiga-Pires & R. G. Grainger, eds, Pioneers in Angiography: the Portuguese School of Angiography, MTP Press Ltd, 1st English edn 1982. There is now a second English edition.

The following American textbooks are now rather old and not easy to get hold of, but are certainly encyclopaedic in scope:

Andre J. Bruwer, Classic Descriptions in Diagnostic Radiology, 2 vols. Charles C Thomas, Springfield, Illinois, 1964.

E. R. N. Grigg, The Trail of the Invisible Light: from X-Strahlen to radio(bio)logy, Charles C Thomas, 1965. A breathless book with an abudance of frustratingly minute illustrations. Good on bibliography.

Ruth and Edward Brecher, The Rays: a history of Radiology in the United States and Canada, Williams and Wilkins, Baltimore, 1969.

There are several biographies of Rontgen, of which the standard is:

Otto Glasser, Wilhelm Conrad Rontgen and the Early History of the Roentgen Rays, with a chapter, Personal reminiscences of W C Roentgen, by Margret Boveri, London, 1933, and Charles C Thomas, 1934.

Smaller and possibly more accessible biographies are:

Otto Glasser, Dr W C Rontgen, Charles C Thomas, 1945, 1958.

A. Hermann, E Streller & R Winau (in German) Wilhelm Conrad Rontgen, 1845-1923, Heinz Moos Verlag, Munchen, & Inter Nationes, Bonn-Bad Godesberg, 1973.

K. T. Claxton, Wilhelm Roentgen, Heron Books, 1970.

BIR Recent additions to the library

Chan, F. L. & Wang, C., 1989. Bailliere's clinical endocrinology and metabolism - International practice and research.

Crues, III J.V., 1991. MRI of the musculoskeletal system

Dodson, M.E., 1991. Transvaginal ultrasound

Eisenberg, B., 1991. Imaging of the thyroid and parathyroid glands

Goldberg, B. & Kurtz, A.B., An atlas of ultrasound measurements

Goldman, S.M. & Gatewood, O.M.B. (Eds)., 1991. CT and MRI of the genitourinary tract

Higgins, C.B., Silverman, N.H. & Kersting-Sommerhoff, B.A., 1990. Congenital heart disease: echocardiography and magnetic resonance imaging

Johnson, R.J., Eddleston, B. & Hunter, R.D. (eds)., 1990. Radiology in the management of cancer

Jones, B.,& Donner, M.W. (Eds)., 1991. Normal and abnormal swallowing imaging in diagnosis and therapy

Lyons, E.A. Practical color atlas of sectional anatomy: Chest, abdomen and pelvis

Mizer, S., Scheller, R.G. & Deye, J.A. (Ed)., 1986. Radiation Therapy Simulation Workbook

BIR LIBRARY

The BIR Library is open weekdays 9 a.m.— 5 p.m. (7 p.m. on Tuesdays and Thursdays).

The journal stock includes more than 100 titles. Though journals may not be taken out of the library, there is a photocopy service, also available by post or FAX. A list of current journals is available on request and is also published in the March and September issues of the Bulletin. Most books (excepting the historial collection) are available on loan.

South West Branch BIR Meeting Report

Dr J.M. Guy, BIR. South West Representative

A meeting was held on 28th June 1991 at Exeter. 23 members were present and Dr Horniblow took the chair. Members stood in memory of Dr Kevin Gaskell.

It was decided that a report of the meeting would be offered to the BIR Bulletin. The relationship between the South West Radiologists' Association and the British Institute of Radiology, south west branch, was debated and it was decided that the present informal relationship should continue. The programme of future meetings was discussed. The next one is to be in Yeovil on 1st November and 1992 meetings will be in Bath on 27th March and in Plymouth in May or June of 1992. This last will be combined with a meeting of SERMO, the Association of Radiologists in Brittany.

At the scientific meeting, papers were presented as follows:

Charles E. Corney - "Urodynamics for the unitiated"

C. Hamilton-Wood - "Doppler ultrasound in the abdomen - Is it worth the effort?"

W. Vennart - "Magnetic resonance imaging - a targetted approach"

C.R. Bayliss - "Put your needle where the money is"

Use of Institute facilities

Readers are reminded of the availability for hire of the Lecture Theatre, Foyer and Library. Affiliated societies are offered a discount.

The Lecture Theatre holds up to 100 people in raked seating and has excellent audio-visual equipment, including VHS video. The Foyer provides space for registration and refreshment breaks for 40 people. The Library, with its beautiful Adams ceiling, can accommodate up to 60 people for refreshment breaks or for an evening reception.

The European Market for Medical Imaging Contrast Media

Report E1515

Contrast Media Erode Financial Constraints

London, September 1991...Europe's medical imaging contrast media market is gradually breaking down the financial barriers which have handicapped its development for many years, and is on target to record year on year growth, according to a new report from international market research publisher Frost & Sullivan.

Pan European sales which had reached an estimated $218 million by the close of 1990, are expected to climb to around $227 million by 1993, and are forecast to reach $237.2 million by 1996.

"Lack of funding and reimbursement problems have in the past limited market growth by restricting the use of non-ionics (low osmolar) products to high risk cases," reveals the report.

"The results of using these products have indicated far higher safety levels than was at first expected, encouraging the relaxation of cost containment restrictions. Low osmolar and non-ionic media are not only increasing at a rate which covers the fall off in ionic usage, but they are also generating new revenue."

The report suggest that there is no future for ionic media in the west European market because many users have already indicated their preference for the new media over ionics regardless of individual risk factors. However, although 90% of users say they wish to see ionics disappear from the market altogether, the report expects the process to be slow.

In terms of product development, exhaustive research and development efforts during the review period are expected to focus on the further reduction of toxicity, improving patient throughput and giving a higher information yield. Other likely areas of improvements are in levels of radiopacity, and the development of tissue-specific and organ-specific agents.

In its analysis of market prospects by revenue, Frost [illegible]an expects sales of ionic media to drop from an estimated $44.2 million in 1990 to around $41.6 million by 1993, and forecasts revenue of only $38.9 million by 1996. By this time the agents can be expected to represent only just over 20% of the iodinated product sector and around 16.4% of the overall market.

Non-ionic media on the other hand, are set to experience steady growth, from an estimated $136.3 million in the report's base year, to a forecast $154.1 million by 1996. By this time, they can be expected to constitute almost 80% of the iodinated segment, and nearly 65% of the overall market.

MRI enhancement agents are likely to represent the fastest growth area with revenue climbing from a relatively small base of $1.7 million in 1990 to a forecast $4.5 million by 1996. Here, growth will be largely fuelled by expansion in the MRI equipment market, and by a growing interest in the use of agents in spinal and body imaging. The sector is unlikely to be handicapped by the agents' relative high unit costs.

In the barium products market, growth is expected to be slow, with the only increases stemming from sales of ancillary products. In particular there will be a continued decline in demand for barium sulphate, predicts Frost & Sullivan.

In its review of the market by country, the report reveals that Germany and France together account for almost six of every 10 contrast media sales. Revenue in the two leading markets stood at an estimated $68 million and $62 million, respectively, in 1990. The other three major markets lag some way behind the leaders. Estimated 1990 revenue from the UK stood at $27 million, from Italy $24 million, and from Spain $16 million. For the road ahead, the UK can look forward to forecast 1996 revenue of $30.6 million, sales in Italy are expected to climb to $25.3 million, and in Spain to $16.5 million.

The price of report E1515 is $3900

For sales information, contact Customer Service, Frost & Sullivan, Sullivan House, 4 Grosvenor Gardens, London SW1W ODH. Tel: 071 730 3438

In the US, contact Customer Service, Frost & Sullivan, 106 Fulton Street, New York, NY 10038. Tel: 212 233 1080

BIR Company Subscriber Scheme

The BIR company subscriber scheme is aimed at all companies with an interest in radiology and allied sciences.

For an annual subscription of £300 p.a. member companies are offered an attractive benefits package. To find out why your company should join the leading edge companies listed below, please contact Mr Tony Hudson, Administration Manager, British Institute of Radiology, 36 Portland Place, London W1N 4AT. Tel: 071-580 4085.

AEA Technology
Wigshaw Lane, Culcheth
WA3 4NE. Tel. 0925-252000 Ext. 4206
Product areas 7, 8.
Contact Mr J. G. Tyror, Director of Safety.

Agfa-Gevaert Ltd
27 Great West Road, Brentford, Middlesex
TW8 9AX. Tel. 081-560 2131.
Product Area 1.
Contact Miss Anne Sparrow.

American Medical Ltd
PO Box 971, London SW10.
Tel. 071-352 8051. Fax: 071-376 4508.
Product areas 1, 3, 4, 5, 7, 8.
Contact Betsy Riley, Managing Director.

Amersham International PLC
Lincoln Place, Green End, Aylesbury,
Bucks HP20 2TP. Tel. 0296 395222.
Product areas 4, 5, 6.
Contact Mr C. M. T. Medley, Sales and Marketing Manager.

Bard Ltd
Forest House, Brighton Road, Crawley,
West Sussex RH11 9BP.
Tel. 0293 527888, ext. 2204.
Product area 2.
Contact Peter Dekkers, Product Manager.

B.M.V.A.
Department of Computer Science,
University of Reading, P.O. Box 220,
Whitnights, Reading RG6 2AX.
Contact Mr G Sullivan, Treasurer.

British Nuclear Fuels plc
Room 525, Hinton House, Risley,
Warrington, Cheshire WA3 6AS.
Tel. 0925 835022.
Product areas 8, 11.
Contact Dr R. J. Berry, Director of Health and Safety and Environmental Protection.

Bruel & Kjaer (UK) Ltd
92 Uxbridge Road, Harrow, Middlesex,
HA3 6BZ. Tel. 081-954 2366.
Product areas 3, 6.
Contatct Mr D. Lewis, Sales Manager.

Calumet Coach Co.
33 Shallbourne Rise, Camberley GU1J
2EJ. Tel. 0276 64490.
Product areas 1, 4, 5.
Contact Mr P. Supple, Managing Director of International Operations.

Cardiac Services Ltd
95A Finaghy Road, South Belfast
BT10 OBY. Tel. 0232-625566.
Product areas 1, 3, 4, 5, 6.
Contact Mr R. J. Brown, Managing Director.

Cea (UK) Ltd
25 Presley Way, Crownhill,
Milton Keynes MK8 0ES
Tel. 0908 263090. Fax: 0908 263546.
Product areas 1, 3, 4, 5, 6.
Contact John Dunster, Managing Director.

Claudius Ash
Summit House, Summit Road, Potters
Bar, Herts, EN6 3EE. Tel: 0707 46433.
Fax: 0707 46429.
Product area 1.
Contact Mr A Calvert-Jones, X-Ray Specialist.

Clinical Press Ltd
Redland Green Farm, Redland, Bristol BS8
7HF. Tel. 0272 420526.
Product area 17.
Contact Dr Paul Goddard, Chairman.

Computer General
5 Greenway Business Park, Bellinger
Close, Chippenham, Wiltshire SN15 1BN.
Tel. 0249 445566. Fax. 0249 445595.
Product areas 1, 10.
Contact Alan Mawdsely, Division Manager/Yvonne Morris, Marketing Manager.

Data-Med Computer Services Ltd
10 Faraday Building, Highfields Science
Park, University Boulevard, Nottingham
NG7 2QP.
Tel. 0602 431431. Fax: 0602 430782.
Product area 13.
Contact Mr C. Fildes, Sales Manager.

Dornier Medical
610 Delta Office Park, Welton Road,
Swindon, SN5 7XF.
Tel. 0793 421771.
Product area 3.
Contact Geoff F[illegible] UK Manager.

Du Pont (UK) Ltd
Wedgwood Way, Stevenage, Hertfordshire SG1 4QN.
Tel. 0438 734000.
Product areas 1, 3, 4, 5, 6, 7, 9 and 10.
Contact Mr E. G. Lovat, Product Manager, Diagnostic Imaging.

E. G. & G. Limited
Vale Road, Windsor, Berkshire SL4 5JP.
Tel. 0753 855611.
Product areas 1, 6, 7, 8.
Contact Mr Roy Hauton, Sales Executive (Therapy).

Elscint (GB) Ltd
Colonial Business Park, Colonial Way,
Watford, Herts WD2 4PT. Tel. 0923 39511.
Product areas 1, 3, 4.
Contact Faith Gorman, Marketing Manager.

E-Z-EM Ltd
1230 High Road, Whetstone, London N20.
Tel. 081-446 9714.
Product areas 1, 2, 8.
Contact Richard Bayliss, Sales and Marketing Manager.

Fuji Photo Film (UK) Ltd
125 Finchley Road, London
NW3 6JH. Tel. 071-586 9351.
Product areas 1, 3.
Contact Mr R. G. Brown, Marketing and Administration Manager.

Gammex-RMI Ltd
34 Shakespeare Street, Nottingham
NG1 4FQ. Tel. 0602 483807.
Product areas 1, 3, 4, 5, 6.
Contact Mr Brian Scott, Commercial Manager.

IBM UK Laboratories Ltd
Scientific Centre, 2-5 St Clement Street,
Winchester, Hants, SO23 9DR.
Tel. 0962-844191.
Product areas 10, 13.
Contact Dr J.M. Knapman, Consultant Scientist.

IGE Medical Systems Ltd
352 Buckingham Avenue, Slough, Berks
SL1 4ER. Tel. 0753 874000.
Product areas 1, 2, 3, 4, 5, 6, 8, 9.
Contact Jill Mitchell, UK Sales Support.

Kodak Ltd
PO Box 66, Station Road, Hemel Hempstead, Herts HP1 1JU.
Tel. 0442 61122.
Product area 1, 3, 4, 6, 8, 9, 12, 13, 14, 15
Contact Mr J. J. G. Tweed, Manager, Health Sciences Division.

Lanmark
PO Box 317, Beaconsfield, Bucks HP9 2LR. Tel. 0494 791615/670586.
Product areas 1, 3, 4, 5, 9, 10, 15, 16.
Contact Liz Beckmann, Director.

3M UK PLC
3M House, Bracknell, PO Box 1, Berks RG12 1JU. Tel. 0344 858000.
Product area 1.
Contact Mr Alan Budge, Marketing Manager.

Mallinckrodt Diagnostica (UK) Ltd
11 North Portway Close, Round Spinney, Northampton NN3 4RQ. Tel. 0604-646132.
Product areas 4, 5.
Contact Mr D. G. L. Wood, Business Manager.

M. A. S. Medical Ltd
Armytage Road, Brighouse, West Yorkshire HD6 1QF. Tel. 0484 721906.
Contact Martin York, Managing Director.

Meadox (UK) Ltd
Matthew House, Matthew Street, Dunstable LU6 1SD. Tel. 0582 605111.
Product area 2.
Contact Mrs Sheila Heap, Sales and Marketing Manager.

Medical Xray Supplies Ltd
Unit 12, Kingsbury Industrial Estate, Church Lane, Kingsbury, London NW9 8AU. Tel. 081-205 9500.
Product area 1.
Contact Mr R. J. Laird, Sales Director/Mr K. Wartnaby, Managing Director.

Mitsubishi Electric UK Ltd
Travellers Lane, Hatfield, Herts AL10 8XB.
Tel. 07072 78756.
Product area 14.
Contact T. F. McCloud, Sales and Marketing Manager.

Nuclear Associates
100 Voice Road, Carle Place, New York 11514-1593, USA. Tel. 516-741 7614.
Product areas 1, 3, 4, 5, 6, 8.
Contact Mr H. Glasser, General Manager.

Nucletron Trading Ltd
Nucletron House, Tarporley Business Centre, Tarporley, Cheshire, CW6 9UY.
Tel: 0829 733611.
Product areas 6, 8.
Contact Mrs Marilyn A. Hart, Office Manager.

Nycomed (UK) Ltd
Nycomed House, 2111 Coventry Road, Sheldon, Birmingham B26 3EA.
Tel. 021-742 2444.
Product areas 1, 3.
Contact Mr L. Birch Hansen, Managing Director.

Oxford Magnet Technology
Wharf Road, Eynsham, Oxford.
Tel. 0865 880880.
Product area 1.
Contact Pauline Hobday, Director of Sales and Marketing.

Philips Medical Systems
Kelvin House, 63–75 Glenthorne Road, Hammersmith, London W6 OLJ.
Tel. 081-741 1666.
Product areas 1, 2, 3, 4, 6, 9.
Contact Mr R. Van der Ploeg, Marketing Manager.

Premise Engineering Ltd
Tibbs Hill Road, Abbots Langley, Watford, Herts WD5 ODR.
Tel. 0923-267433/263320.
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Contact Mr R. K. Beach, Director.

Quantel Ltd
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Radiological Protection Services Ltd
61 Lind Road, Sutton, Surrey SM1 4PP.
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Contact B. H. Cutting, Managing Director.

Schering Health Care Ltd
The Brow, Burgess Hill, West Sussex RH15 9NE. Tel. 0444 232323.
Product areas 1, 2, 3.
Contact Mr Simon Higginbotham or Mr S. Hearne, Product Managers.

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Siemens House, Windmill Road, Sunbury on Thames, Midlesex. Tel. 0932 752334.
Product areas: 1, 2, 3, 4, 6, 8, 9, 10, 13, 14, 15.
Contact L. J. McFadyen, Marketing Assistant.

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Product area 1.
Contact Mrs Annette Drake, Sales Manager

Sony (UK) Ltd
Jays Close, Viables, Basingstoke, Hants RG22 4SB. Tel. 0256 483564.
Product area 14.
Contact Richard Holt, Marketing Manager.

Technical Photo Systems
55 Napier Road, Cumbernauld, Glasgow, G68 OEF. Tel: 0236 739668.
Contact Mr L Thomas, Managing Director.

Toshiba Medical Systems UK
Manor Court, Manor Royal, Crawley, West Sussex RH10 2PY. Tel. 0293 560772.
Product areas 1, 2, 3, 4, 9, 10.
Contact Mr S. M. Weeden, Manager X-ray Products.

Toshiba Medical Systems Europe BV
Schieweg 1, 2627 An Delft, The Netherlands. Tel. 015 61 0121.
Product areas 1, 2, 3, 4, 9, 10.
Contact Mr P Blonk, Office Manager, X-ray BU.

More subscribers overleaf...

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5 Comet House, Calleva Park Estate, Aldermaston, Reading RG7 4QW.
Contact Mr F. Verlaan, Managing Director

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Hampton Court Estate, Summer Road, Thames Ditton, Surrey KT7 OSP.
Tel. 081-398 9911.
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Contact Mr R. B. Wardley, Managing Director.

William Cook (Eur) Ltd
6 Such Close, Letchworth, Hertfordshire SG6 1JF. Tel. 0462 482884 Fax: 0462 480944.
Product area 2.
Contact T. Phizacklea, Product Manager.

Wolters Kluwer U.S. Corporation
c/o Gower Medical Publishing,
Middlesex House, 34-42 Cleveland Str., London W1P 5FB. Tel: 071 636 8300.
Fax: 071 631 3594.
Contact Elly Myers, Marketing Manager.

Wolverson X-Ray
Walsall Street, Willenhall, West Midlands, WV13 2DY. Tel: 0902 637333.
Product areas 1 & 8
Contact Mr R C Lawrence, Managing Director

X-rite (H. Miller Graphics Ltd)
8 Moody Street, Congleton, Cheshire CW12 4AP. Tel. 0260 279988.
Product areas 1, 12.
Contact Mrs P. Dhanani, Medical Sales.

SPECIAL REQUEST

The Muhimbili Medical Centre in Dar-es-Salaam, a university teaching hospital, has requested current radiology textbooks. This department runs the only school of radiology in the country, but it is very difficult to obtain books and those available are very expensive. A list is available on request, but they would be grateful for any titles. If anyone has, or knows of, copies of such books could they please let me know at 12 Turner Close, London NW11 6TU. Collection in north and central London can be arranged.

With thanks, Anne Savage, Honorary Secretary Friends of Overseas Hospital

PRODUCT NEWS

Pioneers of X-ray quality

The X-ray departments at St. George's Hospital, London and Bristol Royal Infirmary have been awarded a prestigious British Standard for their pioneering work on quality management.

For the past 18 months, the X-ray departments have been developing a quality assurance system to meet British Standard 5750. Although the standard is widely used in industry, this is thought to be the first time that it has been awarded to a clinical department.

The idea was first suggested some 2 years ago and the Department of Health funded a research project to facilitate the efforts of the X-ray departments. They were assessed between November 4th and 8th by independent experts in quality management.

Following the award, the Director of Clinical Radiology at St. George's, Dr John Williams said, "Everyone in both our departments is delighted to be awarded the British Standard. It is a tribute to all the hard work that our staff have put in."

"This ensures that we offer a top-class service to patients and their doctors", added Dr Iain Wawtt, Director of Clinical Radiology at Bristol Royal Infirmary.

The certification applies to St. James and Lanesborough Wings and to the A&E X-ray department at St. George's and to the departments at Bristol Royal Infirmary. In both hospitals it covers the clinical radiological, radiographic, nursing and clerical aspects of the service.

New products from Toshiba

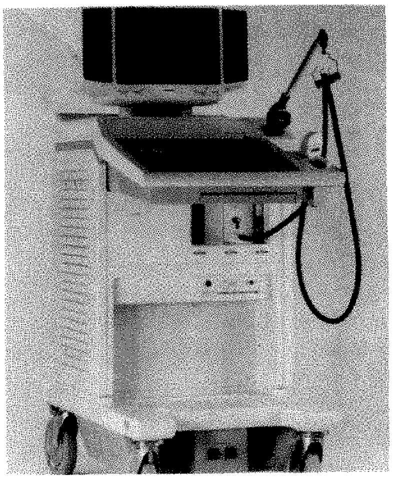
Toshiba Medical Systems has recently introduced some new ultrasound equipment. They include:

● the newest upgrade of the diography system SSH-160A.
The system features many new elements including dynamic colour compression for better colour definition and picture radius independent steering modes for 5 and 7.5 MHz Peripheral Vascular probes.

● The ultrasound system SSH-140A is the newest version of the echocariography ultrasound system SSH-140A.
This mid-range system scans in black and white as well as colour. It has FFT Doppler, pulsed wave doppler and full steerable colour waved Doppler.

● A small sized Biplane TEE probe capable of making longitudinal as well as transversal images of the heart. It can be used with their alpha-series echocardiography ultrasound equipment SSH-160A and SSH-40/C.
Paediatric cardiology can now be performed with anesthetized infants. The movement of the heart can then be observed in two dimensional images as well as colour Doppler. During surgery, the small Biplane TEE probe can be placed in the mouth together with the respirator. It can be used pre-, during post-surgery.

● The SSH-140A/G is a mid-range colour Doppler ultrasound system for routine radiology and OB/GY practice. The SSH-140A/G scans black and white and has FFT as well as colour Doppler. The scanner is easy to use with a touch command screen and full range of pre-set functions.
The system (*featured below*) is also very transportable for examination chambers, bedside use and in emergency care units.



For more information on any of the above products, please contact: Ms A Bromberg, SP/PR Department, Toshiba Medical Systems Europe bv, Schieweg 1, 2627 AN Delft, The Netherlands. Tel: 31 15 610121. Fax: 31 15 622359.

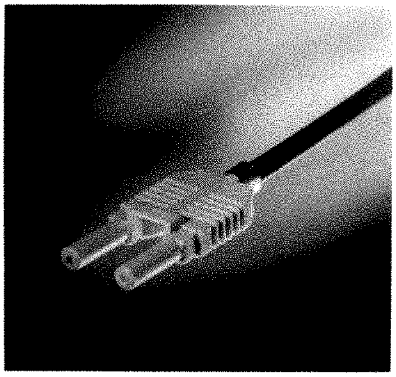
Klinicview from Kontron

Klinicview, a unique patient monitoring network based on advanced fibre optic technology, from Kontron Instruments Limited, uses plastic opical fibres to overcome many of the problems associated with conventional network systems. Klinicview is unaffected by unforseen power surges, and minimises the impact of electromagnetic interference and noise difficulties prevalent in the hospital environment.

At the heart of the system is a unique hub which uses a star to bus configuration. Klinicview is thus a "network within a network", combining the high reliability of a bus network with the high system uptime of a star network. Any faults on the network drivers are confined to the affected components and have no system wide implications - vital if continous data analysis is being performed on networked information. The overriding advantage of Klinicview is its consistancy - and thus its reliability.

Each Klinicview network permits up to 32 beds, four central stations and four additional devices to be connected together for a wide number of viewing options. Separate Klinicview network can be linked to provide larger information transfer systems if required. The initial cost of the system is low and, given its reliability, maintenance overheads can be kept to the minimum.

For further information contact: Kontron Instruments Ltd, Blackmoor Lane, Croxley Centre, Watford, Herts WD1 8XQ. Tel: 0923 245991/56252. Fax: 0923 50146.



Research trust orders Philips MRI system

The Clatterbridge Cancer Research Trust has contracted to purchase a Philips GYROSCAN T5/XPA MRI scanner for a research programme to be carried out at the Mersey Regional Centre for Radiotherapy & Oncology (MRCRO) at Clatterbridge Hospital. The T5/XPA is a powerful mid-field system, providing integrated facilities for MR angiography, real-time multi-planar reformatting and other sophisticated applications.

The contract, which includes all associated building works, is scheduled for completion in approximately 6 months time.

The trust which was set up in 1974 by clinicians at the MRCRO, based at Clatterbridge Hospital with the aim of promoting research into cancer and its treatment, raised the funds for purchase by public appeal for a "Superscanner" (as described in the fund-raising literature). It is continuing to raise monies to fund the ongoing research programme to be carried out by MRCRO on the role of MRI in the diagnosis and management of cancer.

Radio-Pharmaceuticals dispensing work station

A totally enclosed work-station has been launched by ultra clean air and containment specialists Medical Air Technology. It combines the sterility achieved by a vertical downward laminar flow of HEPA filtered air, with the safety of a negative pressure contained work area. The IsoMAT can be fitted with a special generator stand incorporating a lead-lined ^{99}Tc^{m} generator storage drawer.

Labelling and dispensing radio-pharmaceuticals should take place in an environment where radio-active contamination is at an acceptably low level. The same environment must also be controlled to reduce microbial and particle contamination.

For more information, or a copy of the leaflet, please contact: M A T, Canto House, Wilton Street, Denton, Manchester M34 3LZ. Te[illegible]61 320 5652.

BIR Calendar

Unless otherwise indicated, enquiries should be addressed to the Conference Manager, British Institute of Radiology, 36 Portland Place, London W1N 4AT (Tel. 071-436 7807).

Vascular imaging
January 24, 1992
Organizer: Dr J. F. Reidy

The Radiosensitivity of Human Tumours and Normal Tissues — How close to clinical application?
February 11, 1992
Organizer: Dr M. Saunders

Quality standards in nuclear medicine
February 18, 1992
Organizer: Dr A. Smith

3-D image analysis in medical imaging
February 25, 1992
Organizer: Professor M. A. Smith

Megavoltage portal imaging
April 10, 1992
Joint meeting with IPSM
Organizer: Dr W. Jones

Radiology & Oncology '92
18–20 May 1992
International Convention Centre, Birmingham

Computed Radiology - the opportunities
11 June 1992
Scientific Societies Lecture Theatre
Organizers: Mr A Budge, Mrs E Beckman

Measurement Techniques for Ultrasound Exposure
July 1, 1992
Organizer: Dr F. Duck

Conference Services

Is there a seminar, conference or evening get-together you want to organize, but you don't have the time? The BIR Conference Office may be able to help you. Please call Miss Vanessa Whitehead, Conference Manager, to discuss possibilities. Tel: 071-436 7807

Meetings and Courses

Abdominal Interventional Procedure
January 30-31, 1992
London
Further information: The Conference Office, Royal College of Radiologists, 38 Portland Place, London W1N 3DG. Tel: 071-636 4432. Fax: 071-323 3100

MRI Teaching Course
January 30-31, 1992
Manchester
Further information: The Conference Office, Royal College of Radiologists, 38 Portland Place, London W1N 3DG.
Tel: 071-636 4432. Fax: 071-323 3100.

Radiation Dosimetry, Radiation Standards and Dosimetry Protocols
February 4-5, 1992
Teddington, Middlesex
Further details: Miss D H Pritchard, Building 62, Division of Radiation Science and Acoustics, National Physical Laboratory, Queens Road, Teddington, Middlesex, TW11 OLW. Tel: 081-943 6070 or 081-977 3222 ext 6070.

The Barts/London FRCR II Revision Course (MCQs, Film Reporting and Practice Vivas)
February 10-12, 1992
London
Further details: Mrs C Burrage, Course Secretary, Room 26, Dunn Laboratories, St Bartholowmew's Hospital, London EC1A 7BE. Tel: 071-601 7531.

Computed Body Tomography 1992 - The Cutting Edge
February 13-16, 1992
Florida USA
Further details: Programme Coordinator, Johns Hopkins Medical Institutions, Office of Continuing Education, Turner Building, 720 Rutland Avenue, Baltimore, Maryland 21205. Tel: (301) 955-2959.

Head and Neck MRI at the University of L'Aquila
March 2-6, 1991
L'Aquila, Italy
Further details: Prof. R. Passariello, Radiology, Ospedale SM Collemaggio, 1067100, L'Aquila I, Italy. Fax: 39-682410997.

Skeletal Radiology Group of the Royal College of Radiologists
March 5-6, 1992
Coventry
Further details: Dr J Chandy, Consultant Radiologist, X-ray Department, Coventry & Warwickshire Hospital, Stoney Stanton Road, Coventry. Tel: 0203 224055.

Principles and Practice of Clinical MRI
March 5-8, 1992
Florida, USA
Further details: Programme Coordinator, Johns Hopkins Medical Institutions, Office of Continuing Education, Turner Building, 720 Rutland Avenue, Baltimore, Maryland 21205. Tel: 1 (301) 955-2959.

PET and SPECT Imaging of Living Brain Chemistry in Health and Disease
March 11-13, 1992
Maryland, USA
Further details: Program Coordinator, Johns Hopkins Medical Institutions, Office of Continuing Education, Turner Building, 720 Rutland Avenue, Baltimore, Maryland 21205, USA. Tel: 1 (301) 955-2959.

Study Day on Management of Pancreatic Cancer
March 24, 1992
University of Southampton
Further details: Mrs J Daniels, University Surgical Unit, F Level Centre Block, Southampton General Hospital, Tremona Road, Southampton, SO9 4XY. Tel: 0703 796144. Fax: 0703 794020.

International Symposium on Recent Advances in Diagnostic Imaging and Radiation Oncology
March 24-27, 1992
Kathmandu, Nepal
Further details: Dr Naresh Prasad, Dept. of Radiology, Baylor College of Medicine, Houston, Texas 77030, USA. Tel: (713) 798 4415. Fax: (713) 798 5556.

The Cambridge meeting on Chest Disease
March 25-27, 1992
Cambridge
Further details: Dr C D R Flower,\
Department of Diagnostic Radiology, Addenbrooke's Hospital, Hills Road, Cambridge CB2 2QQ. Tel: 0223 216203.

24th International Diagnostic Course in Davos - ABDOMEN
March 28-April 3, 1992
Davos, Switzerland
Further details: IDKD, PO Box 224, CH-8028, Zurich, Switzerland. Tel: 01 262-2404.

The Biological and Epidemiological Bias for Radiation Protection Standards
April 1-2, 1992
Oxford
Further details: Dr D N S Dixon, Programme Committee Secretary, The Society for Radiological Protection, 67 Oatlands Park, Linlithgow, West Lothian EH49 6AS. Tel: 031-244 2779.

6th Symposium Mammographicum
April 1-3, 1992
London
Further details: The Conference Office, The Royal College of Radiologists, 38 Portland Place, London, W1N 3DG. Tel: 071-636 4430. Fax: 071-323 3100.

Institute of Biology National Conference: Biology in Europe after 1992
April 2-3, 1992
Southampton
Further details: Andrea Silvester or Nicola Beaney, Institute of Biology, 20 Queensberry Place, Loindon SW7 2DZ. Tel: 071-581 8333.

Eurodop '92: Major International Symposium on the Medical Applications of the Doppler Effect in Diagnostic Ultrasound
April 5-8, 1992
Brighton
Further details: Eurodop '92, Bell Howe Conferences, 1 Willoughby Street, Beeston, Nottingham NG9 2LT. Tel: 0602 436323.

Two-day workshop on Electronic Portal Imaging.
April 3-4, 1992
California, USA.
Further details: Dr Norman A Baily, Department of Radiology 0632, University of California, San Diego, 9500 Gilman Drive, La Jolla, CA 92093-0632. USA.

European Society of Gatro Intestinal Radiologists 3rd Annual Congress
22,23-24 June, 1992
Nice, France
Further details: Professor J M Bigot, Radiologist des Hopitaux, Hopital TENON 4, rue de la Chine, 75970, Paris.

The 3rd AFSUMB '92: The 3rd Congress of Asian Federation of Societies for Ultrasound in Medicine and Biology
August 30-September 3, 1992
Seoul, Korea
Further details: Dr. Byung Ihn Choi, Department of Diagnostic Radiology, Seoul National University Hospital, 28 Yongon-Dong, Chongno-Gu, Seoul 110-744, Korea
Tel: (822) 766-0930. Fax: (822) 766-0950

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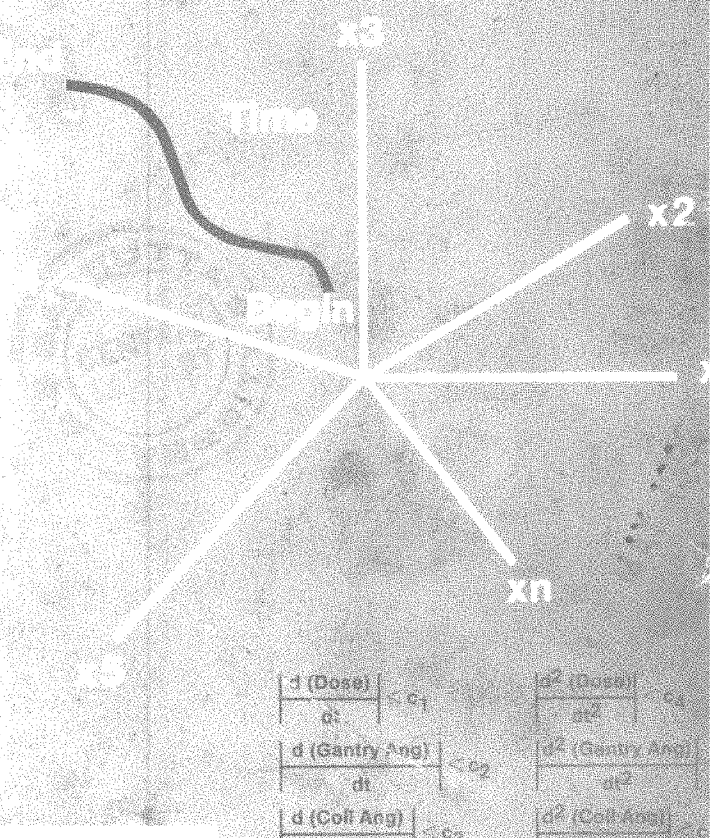
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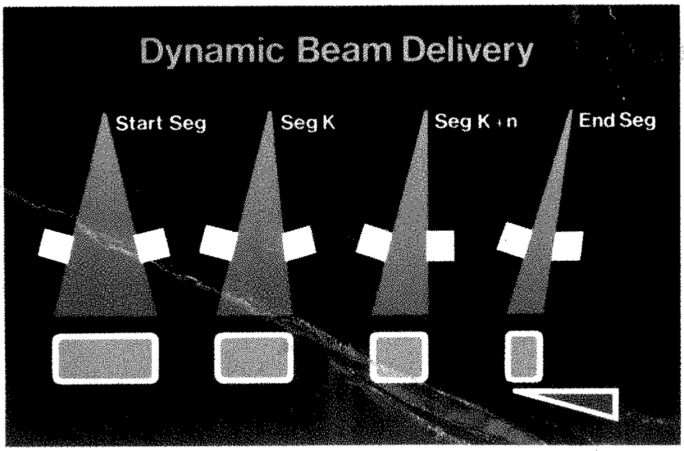

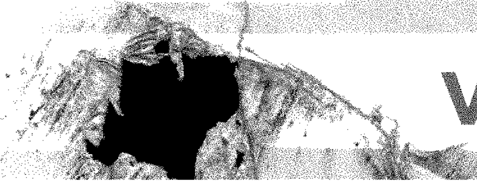

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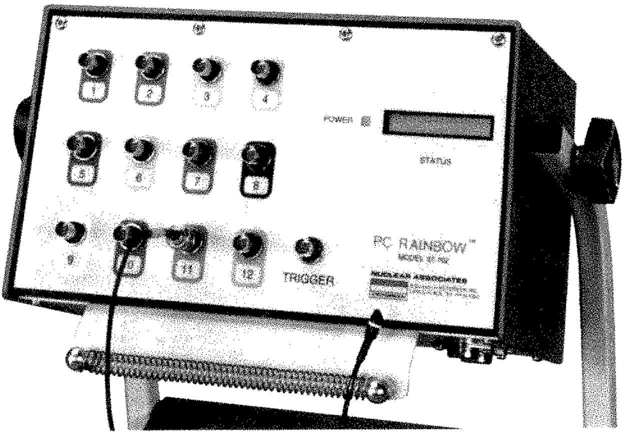

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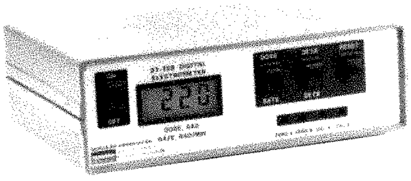

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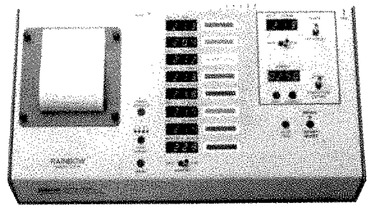

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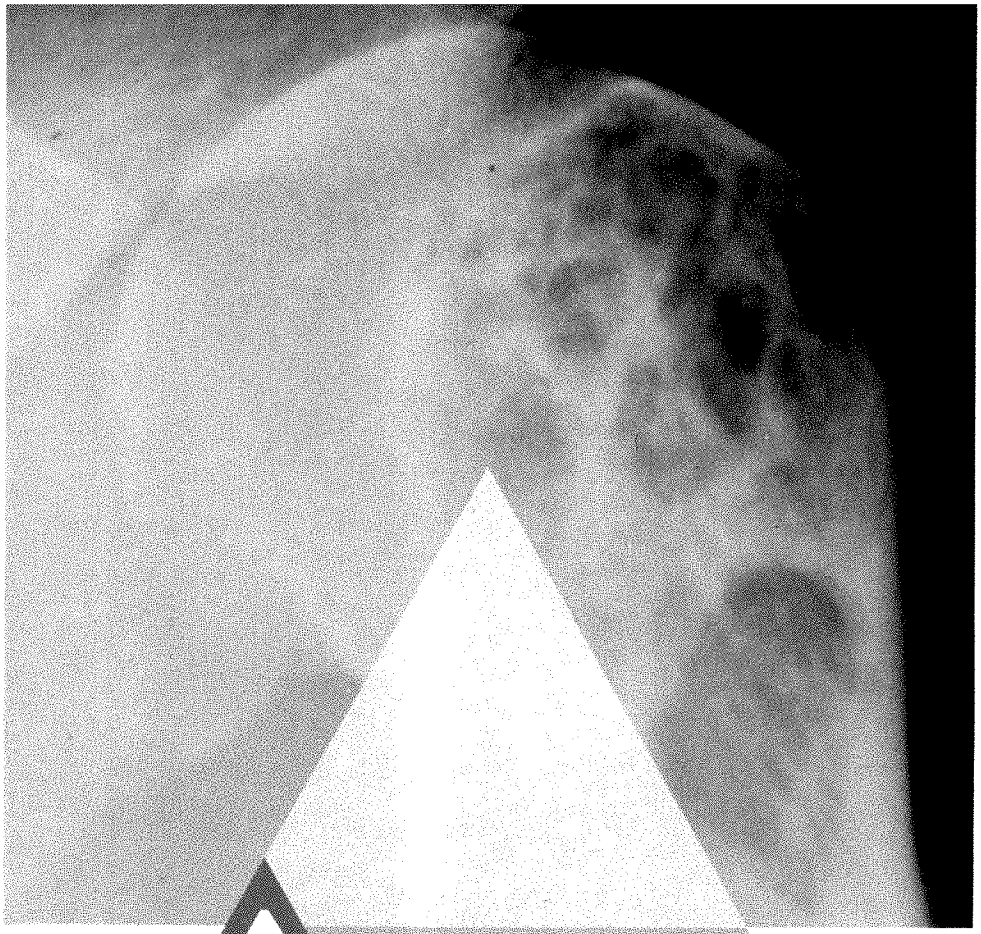

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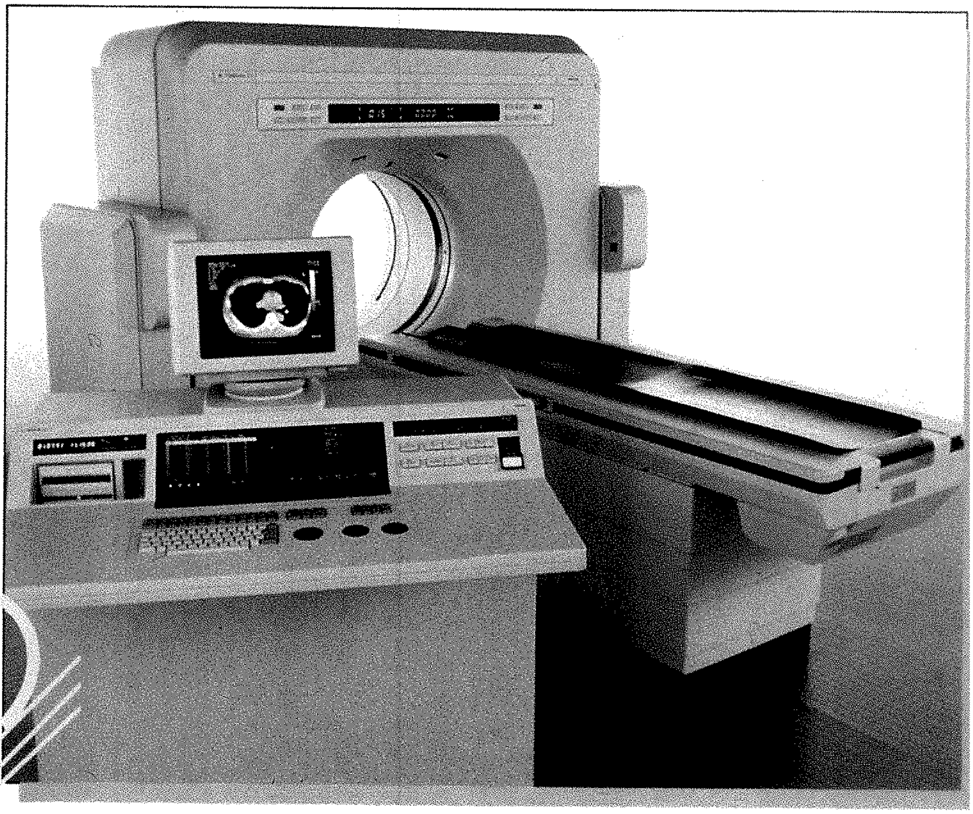

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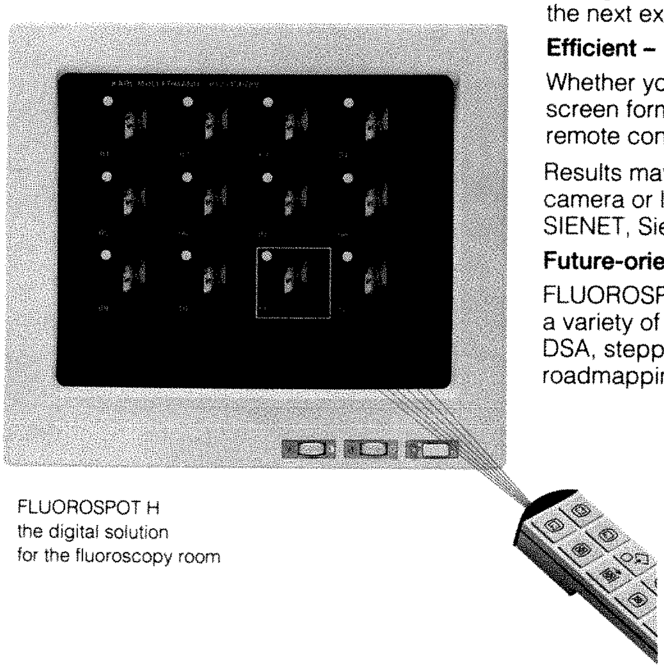

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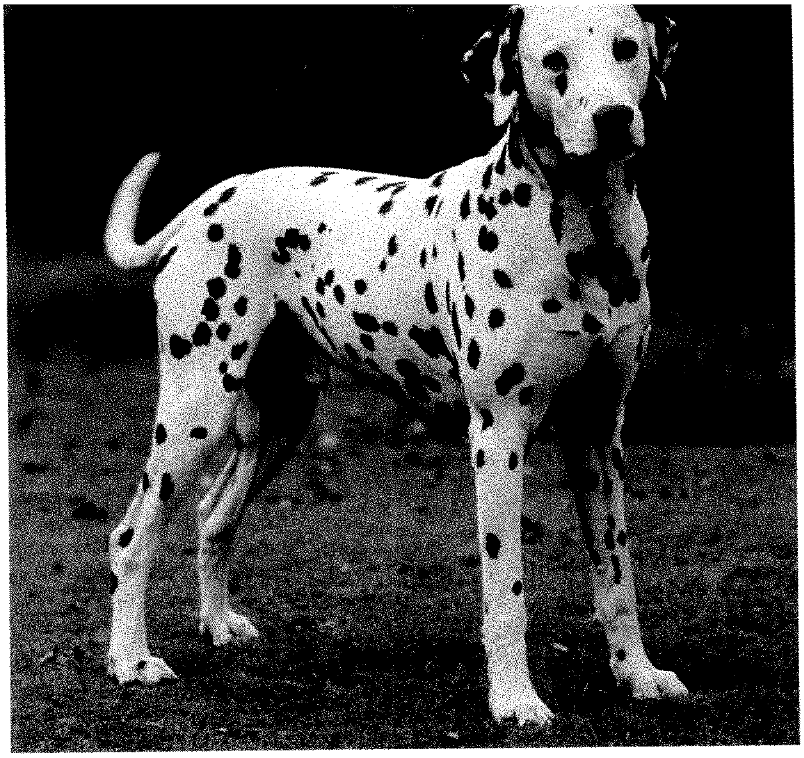

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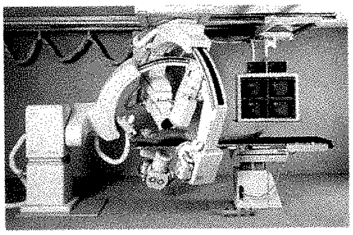

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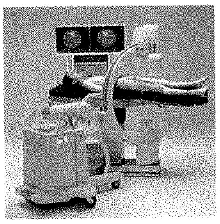

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Computed tomographic assessment of soft tissue abnormalities following calcaneal fractures

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(*Received 10 January 1991 and in revised form 26 July 1991, accepted 6 August 1991*)

Keywords: Calcaneum, Fracture, Computed tomography

Abstract. Computed tomographic (CT) examinations of 50 acute calcaneal fractures were compared with a further series of 77 fractures in which the date of injury preceded the CT by 6 months or more. 42 (84%) of the fractures in the acute group and 55 (71%) in the chronic group were classified as intra-articular and they form the basis of this study. The alteration in the position of the peroneal tendons in the two groups was similar, with a 5% or less difference in each category. In the acute group the peroneal tendons were normally located in 40.4% of the cases, entrapped by bone in 11.9%, subluxed in 33.3% and dislocated in 14.2%. Structural abnormalities of the peroneal tendons and surrounding soft tissues were identified in 52.4% of the acute group and in 61.1% of the chronic group. The incidence of partial rupture of the peroneal tendons in the chronic group was approximately one third that in the acute group, but the low incidence of complete tendon rupture remained unchanged. The inference from these observations is that, in the majority of cases, partial peroneal tendon rupture is reversible, whereas complete rupture is not. Seven fractures were common to both series and from this limited group the identification of haemorrhage around the peroneal tendons in the acute phase was shown not to be related to the subsequent development of chronic stenosing tenosynovitis. Various abnormalities of the medial tendons of the hindfoot were identified in 17% of the acute group and in 18% of the chronic group. Following calcaneal fracture, CT in both the immediate post-fracture period and in the late phase can be used to detect and classify the soft tissue changes. The limitations of comparing the two groups in this study are discussed.

When dealing with musculoskeletal trauma, there is a tendency for the attending clinician and radiologist to concentrate on the bony abnormalities and overlook the associated soft tissue injuries. Many of the numerous articles published on the use of computed tomography (CT) in the evaluation of acute calcaneal fractures deal principally with fracture patterns illustrated by CT scans imaged on a bone window and only make a brief comment on soft tissue involvement (Guyer et al, 1985; Heger et al, 1985; Pablot et al, 1985; Segal et al, 1985; Gilmer et al, 1986; Hindman et al, 1986; Heuchemer et al, 1988; Lowrie et al, 1988; Crosby & Fitzgibbons, 1990). A few recent studies have emphasized the role of CT in the assessment of tendon trauma following acute calcaneal fractures (Rosenberg et al, 1987) and in their longterm follow-up (Bradley & Davies, 1990), as well as in other soft tissue afflictions of the hindfoot (Rosenberg et al, 1986, 1988a, 1988b, 1988c; Keyser et al, 1988). The purpose of this paper is both to study prospectively with CT the soft tissue changes around the hindfoot in a group of patients presenting with an acute calcaneal fracture, and to compare the findings with a second group on whom CT examination was performed more than 6 months after sustaining the injury.

Patients and methods

High resolution CT of the hindfeet was performed on either a Siemens DRH or CR Whole Body Scanner in both the coronal and the axial planes (Smith & Staple, 1983) on a series of 40 patients who had presented with an acute calcaneal fracture within the previous 2 weeks. Contiguous slices measuring 4 mm were obtained and viewed on bone and soft tissue window settings. The CT examinations were subsequently reviewed and observations regarding bone and soft tissue changes recorded.

The abnormalities in this acute group were compared with the findings in a second group of 67 patients with calcaneal fractures sustained more than 6 months before CT examination. The majority of the cases in this latter chronic group have been the subject of a study published previously (Bradley & Davies, 1990) and are included in the current paper for the purposes of comparison.

CT abnormalities of the soft tissues of the hindfoot were classified either as alterations in the position of the tendons or as alterations in the structural appearances of the tendons and surrounding soft tissues. A normal tendon appears as a well defined, homogeneous,

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rounded density of higher attenuation than muscle and is accentuated by surrounding fat. Obliteration of this fat by a soft tissue density indicates either haemorrhage/granulation tissue in the acute phase, or the scar tissue of chronic stenosing tenosynovitis in the late phase. Distension of the synovial sheath by a halo of low density fluid is characteristic of chronic tenosynovitis. Increased girth of the tendon with heterogeneous areas of decreased attenuation within the tendon substance indicates a partial rupture, whereas a complete rupture is detected by an absence of a portion of the tendon with the defect either replaced by fat or fluid (Rosenberg et al, 1988a; Bradley & Davies, 1990).

Results

A total of 50 calcaneal fractures were identified in 40 patients of the acute group and 77 fractures were identified in 67 patients of the chronic group. There were 32 (80%) male patients and 8 (20%) female patients in the acute group and 48 (72%) males and 17 (28%) females in the chronic group. The age range in the acute group was 19–81 years with a mean age of 44 years. The age range in the chronic group was 12–83 years with a mean age of 48 years.

The plain film incidence of the different types of calcaneal fracture are summarized in Table I according to the Schmidt and Weiner modification of the Rowe and Essex-Lopresti classifications (Essex-Lopresti, 1952; Rowe et al, 1963; Schmidt & Weiner, 1982). 42 (84%) fractures in the acute group and 55 (71%) in the chronic group were categorized as intra-articular fractures, with involvement of the posterior subtalar joint (Types 4, 5a & 5b of Table I). The remainder of this paper is confined to this intra-articular fracture category.

The position of the peroneal tendons for both groups are shown in Figure 1 and illustrated in Figure 2. Structural changes of the peroneal tendons were identified in 22 (52.4%) patients in the acute group and 34 (62%) patients in the chronic group. A breakdown of these changes is shown in Figure 3 (a & b). In all five acute fractures in which haemorrhage alone was identified around the peroneal tendons, the tendons were also shown to be either subluxed or dislocated (Fig. 4a). In nine of the 16 cases in which there was partial rupture of the peroneal tendons, with or without surrounding haemorrhage, the tendons were also shown to be either subluxed or dislocated. Structural changes in or around the peroneal tendons were present in 14 of the 20 acute cases with subluxation or dislocation of the tendons (Fig. 4a & c). Almost half the acute fractures exhibited lateral bony spur formation impinging on the peroneal tendons (Fig. 5), best shown on axial CT. This feature was common in those cases in which the peroneal tendons were trapped by bone in their normal anatomical position. There was otherwise no relationship between the lateral spur formation and the appearances of the peroneal tendons and the surrounding soft tissue.

Table I. Calcaneal fractures: classification and incidence (Schmidt and Weiner modification of Rowe and Essex-Lopresti classifications), after Berquist & Johnson, 1989

Type	Published incidence (%)	Acute group (%)	Chronic group (%)
1a (tuberosity)	6	6	11.7
1b (sustentaculum)	3		
1c (anterior process)	15	2	9.1
1d (infero-lateral)	1		1.3
2 (Achilles avulsion)	4		2.6
3 (linear extra-articular)	19	8	3.9
4 (linear intra-articular)	10–26		3.9
5a (tongue depression)	5	28	29.8
5b (joint depression)	43–60	56	37.7

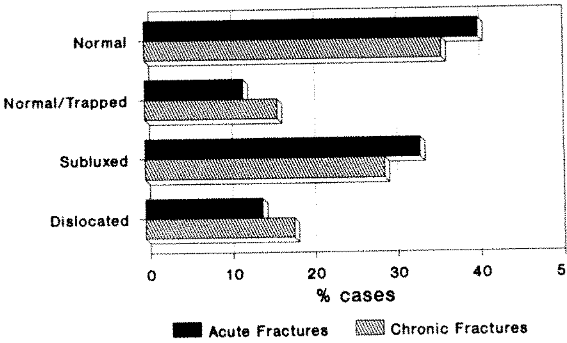


Figure 1. Position of the peroneal tendons.

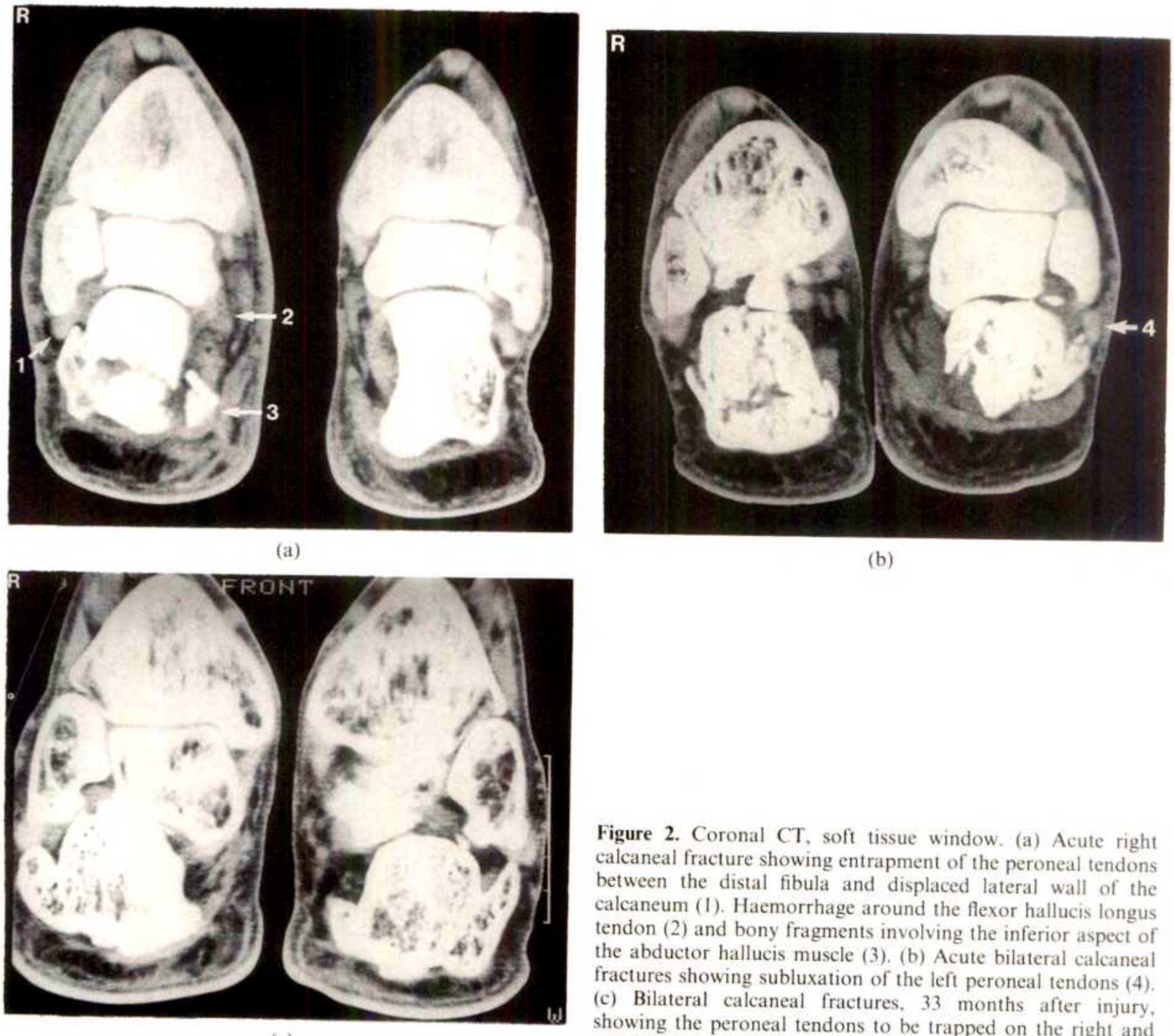
Medially, in the acute group, bony encroachment on the abductor hallucis longus muscle was revealed in four cases, partial rupture of the flexor hallucis longus tendon in two cases and complete rupture of the tibialis posterior tendon in one case. In the chronic group, there was scarring surrounding the flexor hallucis longus tendon in five cases, bony encroachment in two cases and rupture in one case. Rupture of both the flexor hallucis longus and flexor digitorum longus tendons was detected in one case and scar tissue surrounding the tibialis posterior tendon was also detected in one case.

In a minority of acute cases further soft tissue injury to the ankle was identified by an ankle joint effusion or superficial haemorrhage adjacent to the lateral malleolus (Fig. 6).

Four patients with seven intra-articular fractures were common to both the acute and chronic groups in this study. In one case normal peroneal tendons were present bilaterally on both CT examinations. In one case extensive haemorrhage surrounding the peroneal tendons largely resolved to reveal intact tendons (Fig. 7). In one case scar tissue developed around previously normal peroneal tendons and in another case partial rupture of the peroneal tendons persisted on the second CT examination.

Discussion

The literature on calcaneal fractures is confusing regarding which factors are significant or of prognostic

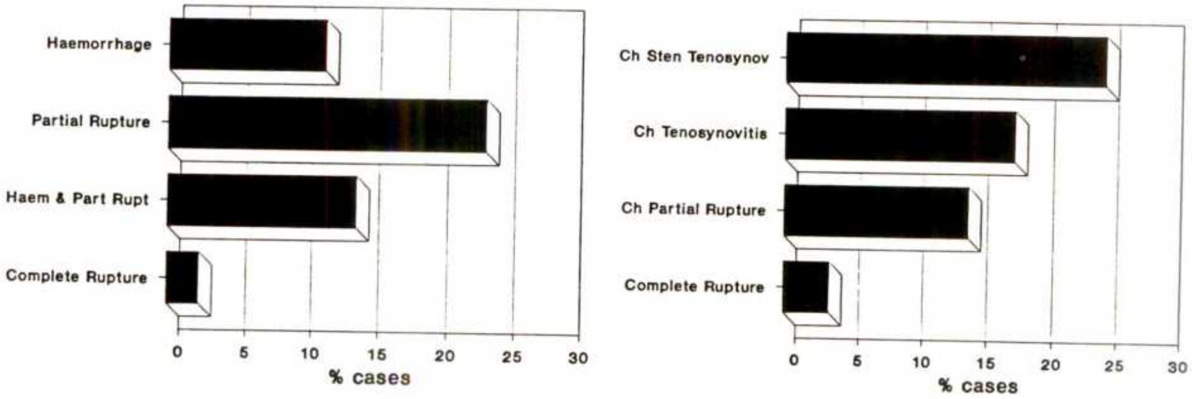


(a)

(b)

(c)

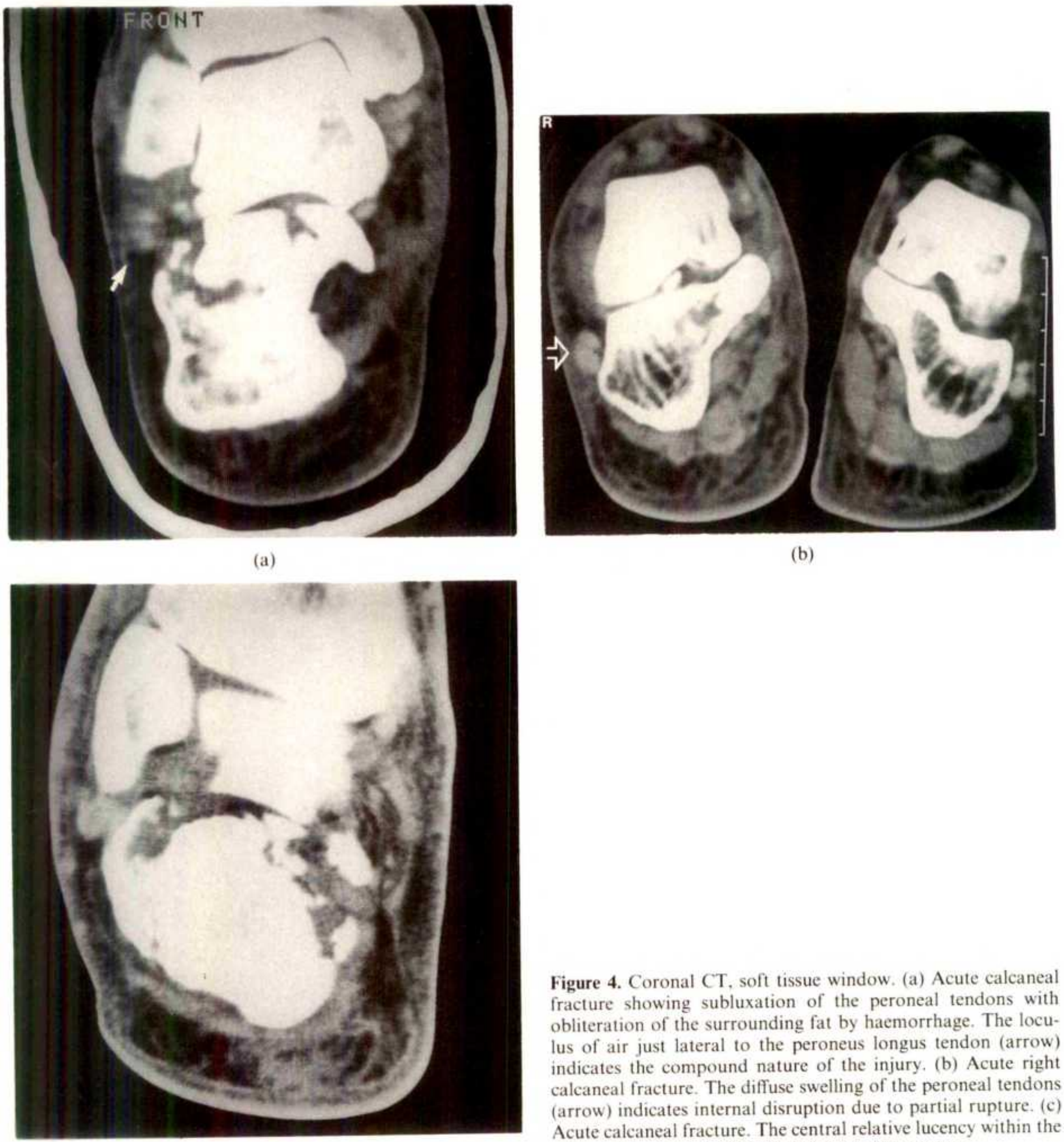
Figure 2. Coronal CT, soft tissue window. (a) Acute right calcaneal fracture showing entrapment of the peroneal tendons between the distal fibula and displaced lateral wall of the calcaneum (1). Haemorrhage around the flexor hallucis longus tendon (2) and bony fragments involving the inferior aspect of the abductor hallucis muscle (3). (b) Acute bilateral calcaneal fractures showing subluxation of the left peroneal tendons (4). (c) Bilateral calcaneal fractures, 33 months after injury, showing the peroneal tendons to be trapped on the right and dislocated on the left.



(a)

(b)

Figure 3. Structural changes in and around the peroneal tendons in the acute (a) and chronic (b) groups.



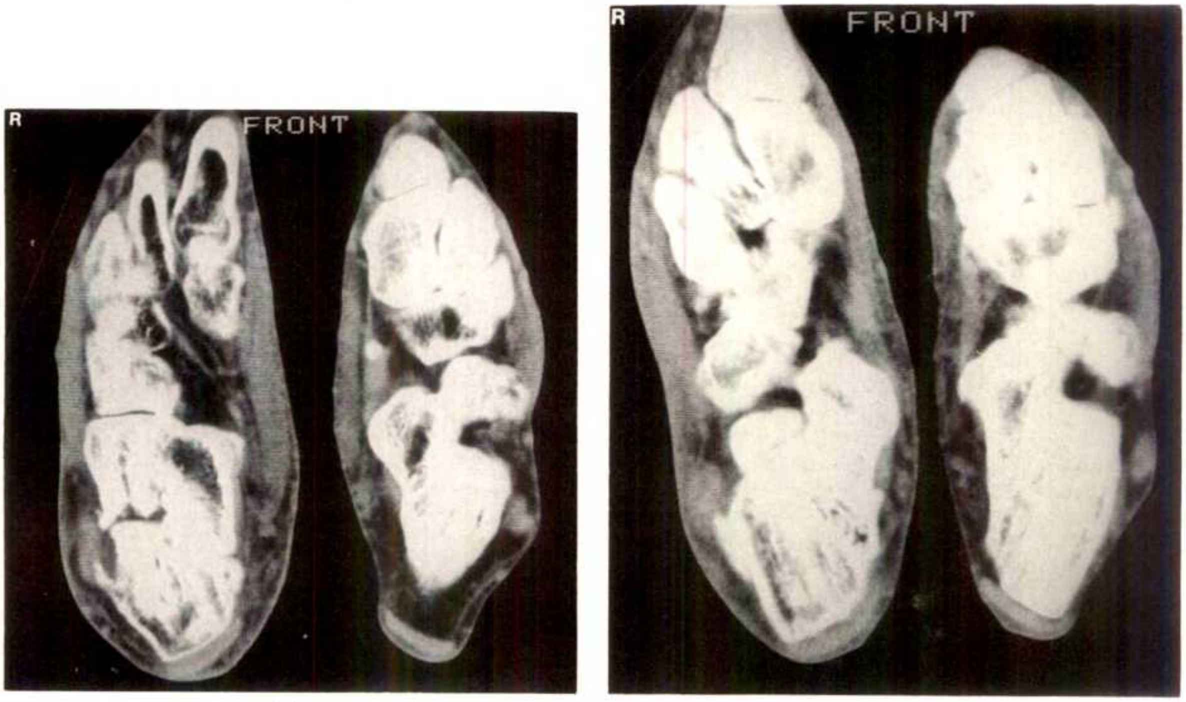
(a)

(b)

(c)

Figure 4. Coronal CT, soft tissue window. (a) Acute calcaneal fracture showing subluxation of the peroneal tendons with obliteration of the surrounding fat by haemorrhage. The loculus of air just lateral to the peroneus longus tendon (arrow) indicates the compound nature of the injury. (b) Acute right calcaneal fracture. The diffuse swelling of the peroneal tendons (arrow) indicates internal disruption due to partial rupture. (c) Acute calcaneal fracture. The central relative lucency within the subluxed tendon sheath indicates complete rupture.

value to the final outcome (Paley & Hall, 1989). Whilst post-traumatic osteoarthrosis of the posterior subtalar joint is arguably the principal cause of morbidity following an intra-articular fracture, another major, longterm complication is injury to the peroneal tendons (Slatis et al, 1979). At the time of injury the downward force of the talus will split the calcaneum into two major fragments. The resultant flattening, with outward splaying of the lateral wall, will displace and damage the peroneal tendons (Palmer, 1948; Essex-Lopresti, 1952). Before the introduction of CT and magnetic resonance imaging (MRI), damage to the peroneal tendons could be either inferred by lateral broadening of the calcaneum or directly visualized by peroneal tenography (Rosenberg et al, 1987). This latter technique is rarely used as it is invasive and difficult to perform in the acute phase when the ankle may be grossly swollen and the tendons displaced. In contrast, CT of the hindfeet is



(a) (b)

Figure 5. Axial CT, soft tissue window. (a) Acute right calcaneal fracture with a lateral spur impinging on the peroneal tendons which are swollen and of decreased attenuation indicating internal disruption. (b) Old right calcaneal fracture, 18 months after injury, showing similar appearances to (a).

relatively non-invasive, easy to perform, allows simultaneous assessment of bony and soft tissue structures and can be undertaken in the presence of an external cast. An additional advantage in a patient with a unilateral fracture is that CT of the uninvolved foot, examined simultaneously, can act as a normal control. The confidence with which observations can be made from CT regarding soft tissue abnormalities of the hindfeet is largely a result of the work originating from one institution which, in many instances, included surgical correlation (Rosenberg et al, 1986, 1987, 1988a, 1988b, 1988c).

This series, comprising 107 examinations, is to the authors' knowledge, the largest published CT study on calcaneal fractures. The results of the acute intra-articular fracture group agree in many respects with the findings of Rosenberg et al (1987). Bony entrapment of the peroneal tendons was present in 11.9% of the current acute group (Fig. 1) and in 13% of Rosenberg's group. However, Rosenberg identified subluxation or dislocation in only 25% of cases, as opposed to 47.5% in this study (Fig. 1). This discrepancy may be explained, in part, by the fact that in this study there was no distinction between lateral displacement and subluxation of the tendons. Haemorrhage or early scar tissue around the peroneal tendons was present in 21% of Rosenberg's cases as compared with haemorrhage, with or without partial tendon rupture, in 26.2% of the current acute series (Fig. 3a). Rosenberg and his colleagues did not identify any structural changes within the peroneal tendons, whereas the current study concluded that partial or complete rupture was present in 40.5% of cases (Fig. 3a). This may be caused by the

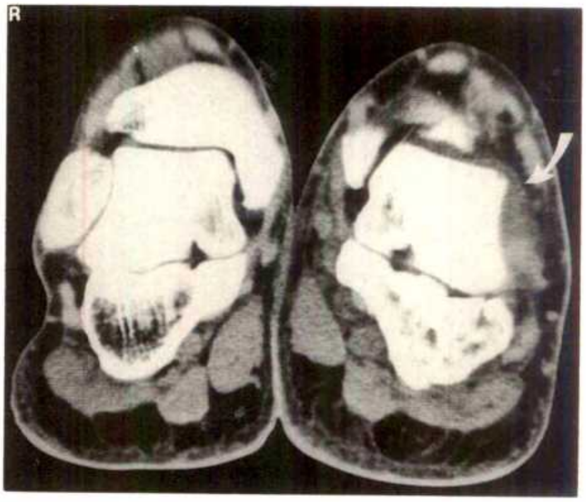
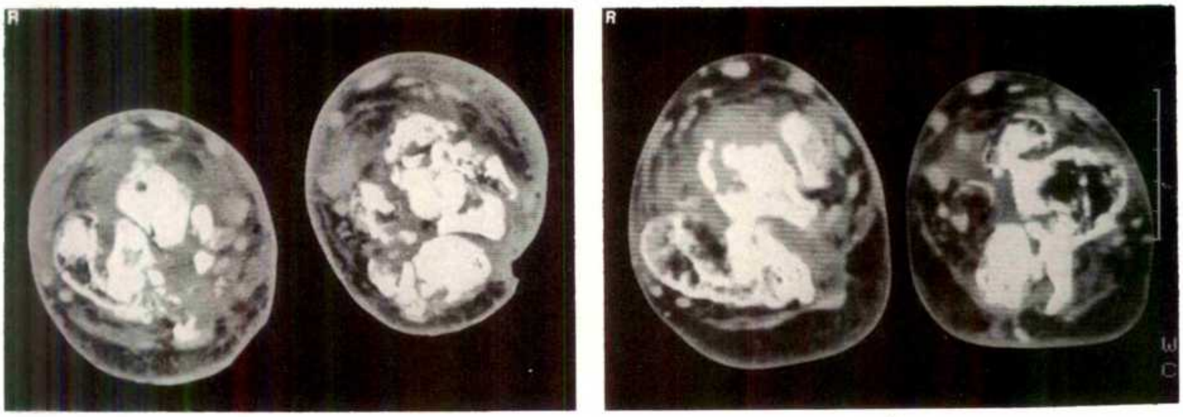


Figure 6. Coronal CT, soft tissue window. Acute left calcaneal fracture showing an ankle joint effusion (arrow) and minor haemorrhage around the peroneal tendons.



(a) (b)

Figure 7. Coronal CT, soft tissue window. Gross bilateral calcaneal and talar fractures. In the acute phase (a) many of the tendons are surrounded by haemorrhage. (b) 8 months later scar tissue is present but many normal tendons are visible surrounded by fat.

fact that their original paper was one of the earlier publications concerning CT of tendons and, with only few exceptions, their patients were examined in the axial plane alone (Rosenberg et al, 1987). The authors of the current study do not consider themselves guilty of the overenthusiastic identification of peroneal tendon rupture in light of the more recent literature on the subject (Rosenberg et al, 1988a, 1988b, 1988c).

In this study, only a limited comparison of the two groups is possible, as they are not identical in a number of respects. The principal difference is the bias in patient selection. All those patients presenting with an acute calcaneal fracture during the study period underwent CT routinely, whereas the chronic group represents the one third of patients who had agreed to attend for CT following receipt of a written request. Nevertheless, the age range, sex ratio and incidence of the various types of fracture (Table I) do suggest that there are moderate similarities. In particular, the position of the peroneal tendons in patients with intra-articular fractures is remarkable similar for both groups, with less than 5% variation in any of the four categories (Fig. 1).

The incidence, in the chronic group, of chronic partial tears of the peroneal tendons of approximately one third that in the acute phase (Fig. 3) would indicate that, in the majority of cases, this change is reversible. A similar incidence of complete tendon rupture in the two groups suggests the contrary (acute group = 2.4%, chronic group = 3.6%). However, the numbers involved are small and there is no conclusive proof in this study that the cases of complete rupture in the chronic group were sustained at the time of the injury. It is likely that many of those patients eligible for the chronic group who declined the invitation to attend for CT were asymptomatic. The majority who did attend were probably motivated by pain and disability, hence the higher incidence of structural changes in the chronic group relative to the acute group.

It might be expected that haemorrhage around the peroneal tendons in the acute group (26.2%) (Fig. 4a) would pre-dispose to scar tissue formation (chronic stenosing tenosynovitis) in the chronic group (25%) (Fig. 3). No such association was found either by Rosenberg et al (1987) in their limited follow-up of 10 cases or in the two cases in the current study, common to both groups, which exhibited these features (Fig. 7).

Abnormalities of the medial tendons were considerably less common than those affecting the peroneal tendons and were found in 17% and 18% of the acute and chronic cases, respectively. This lower incidence reflects the mechanism of injury in that the anteromedial fragment of the calcaneum, including the sustentaculum, usually remains reduced to the undersurface of the talus without injuring the medial tendons, whereas the postero-lateral fragment displaces laterally thereby damaging the adjacent peroneal tendons. However, damage to the medial tendons does occur and can be demonstrated by CT (Carr, 1990).

This study confirms that in both the immediate post-fracture period and long after injury CT may be used to detect soft tissue injuries. Whilst haemorrhage around the peroneal tendons appears to be of limited significance and two thirds of peroneal tendon ruptures probably resolve, a full longitudinal study would be necessary to categorize which soft tissue changes are ultimately of definite prognostic significance.

There remains considerable controversy regarding the treatment of calcaneal fractures; operative or non-operative. The ability of CT to demonstrate both bony and soft tissue abnormalities means that the technique is of value to the proponents of both modes of management. Three-dimensional CT reconstructions may improve the surgeon's visualization of the fractures before operation (Carr et al, 1990; Allon & Mears, 1991) and direct measurements from CT of calcaneal deformity can be used to assess the surgeon's success in restoring the anatomical congruity of the bony structures (Frahm et al, 1989; Krause & Hedtler, 1990). With regards to the soft tissue injuries, MRI may be preferred because of its superior soft tissue contrast resolution (Zeiss et al, 1991), but CT remains an excellent alternative when financial considerations and availability limit access to MRI (Rosenberg et al, 1988a).

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The use of a chelating derivative of alpha melanocyte stimulating hormone for the clinical imaging of malignant melanoma

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Abstract. A novel chelating derivative of alpha melanocyte stimulating hormone, bisMSH-DTPA, has been used for the diagnostic targeting of malignant melanoma. 15 patients were investigated of whom nine were shown by other means to have active disease at the time of the scan. Tumours were imaged in all of these nine patients. Of a total of 46 lesions over 10 mm encountered, 41 (89%) were imaged. There were no false positives and in two cases bisMSH-DTPA was instrumental in reversing diagnoses made using ultrasound. Derivatives of melanocyte stimulating hormone may be of considerable value in targeting melanomas.

The concept of using targeted radioisotopes for the diagnostic imaging of melanoma is not new. Hitherto, however, most efforts have concentrated on the use of monoclonal antibodies, directed towards those cell-surface proteins that are considered to be specific to the tumour. Using such methods, a high degree of diagnostic accuracy can be obtained. For example, in a recent multicentre trial using NR-ML-O5, a murine antibody to the 250 kD proteoglycan melanoma-associated antigen (Salk et al, 1988), 82% of tumours over 3 cm in diameter were detected and similar results were obtained using Fab fragments of other antibodies to the same antigen (Eary et al, 1989; Lamki et al, 1990).

Despite these impressive data, difficulties remain. The injection of murine antibodies is accompanied by the generation of antimurine antibodies in the majority of patients (Blottiere et al, 1990; Lamki et al, 1990) and toxic effects (Dillman et al, 1988) in a significant minority. Other limitations include the reproducibility and stability of labelling (Paik et al, 1985) and the relatively slow rate of penetration of tumour tissue by these large macromolecules (Kwok et al, 1988; Ong & Mattes, 1989).

An alternative approach is to use the naturally occurring receptors for alpha melanocyte stimulating hormone (MSH), which are detectable on the majority of human melanomas (Ghanem et al, 1988; Tatro et al, 1990). MSH is a tridecapeptide with a molecular weight of 1665 D, whose sequence is conserved in all mammalian species so far examined (Eberle, 1988a). It might therefore be expected to be invisible to the immune system and capable of rapid diffusion through tissues.

We have recently synthesized a chelating derivative of MSH, consisting of two complete MSH sequences linked by their *N*-termini to a single molecule of diethylenetriamine pentaacetic acid (DTPA). This compound (bisMSH-DTPA) bound indium-111 stably, was equipotent with the native hormone in the tyrosinase assay and was capable of targeting to the murine melanotic melanoma, Cloudman S91, *in vivo* (Bard et al, 1990a). This paper reports a Phase-I trial in which the usefulness of this compound for the clinical diagnostic imaging of melanomas is examined.

Materials and methods

Chemicals and reagents were of the purest grades commercially available. Indium-111 trichloride (specific activity > 0.37 MBq pg^{-1} of indium) was obtained from Amersham International plc, UK. Metal and pyrogen-free citrate buffer, 0.1 M, pH 5.6, was prepared as previously described (Bard et al, 1990a), sterilized by ultrafiltration (pore size of filter < 0.2 μm) and stored at 4–7° C until needed.

BisMSH-DTPA

BisMSH-DTPA was prepared as a custom synthesis by Cambridge Research Biochemicals (CRB), Northwich, UK (Bard et al, 1990a). The material provided by CRB contained trace amounts of trifluoroacetate present as a counterion associated with basic residues on the peptide. Acetate was substituted for this counterion by reverse-phase chromatography (Gabriel, 1987). The peptide was shown to be homogeneous by HPLC and each batch was checked for the absence of pyrogens by Wickham Laboratories, Fareham, UK. BisMSH-DTPA was dispensed into pyrogen-free vials (0.5 mg, 14 nmol/vial) and stored desiccated at −20 °C.

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Preparation of ^{111}In bisMSH-DTPA

One millilitre of citrate buffer was added to each vial followed by 40 MBq ^{111}In. Metal syringe needles were not used since metal ions dissolved from these had previously been shown to interfere with chelation of indium to bisMSH-DTPA. Each vial was then allowed to stand for at least 30 min at 37° C to ensure complete chelation (Bard et al, 1990a). The preparation was resterilized by ultrafiltration before use and diluted with physiological saline to a total volume of 500 ml.

Patients

15 patients with biopsy-proven melanoma presenting with confirmed or suspected metastatic melanoma were studied. The patients were receiving treatment in the Department of Clinical Oncology and Radiotherapeutics or the Department of Plastic Surgery at Addenbrooke's Hospital, Cambridge, UK and all gave written informed consent to the procedures. The project was approved by the local ethical committee and the radionuclide administration by ARSAC.

Clinical protocol

Patients were infused 0.5 mg (14 nmol) bisMSH-DTPA complexed with 40 MBq ^{111}In over a period of 30 min with the patient lying down. Total body radioactivity was measured by a collimated probe with the patient at 3 m. Readings were taken shortly after injection, at 4 h, 24 h and, in five cases, at 48 h (Cases 1, 3, 9, 10 and 14). Quantitative whole-body scans were taken anteriorly and posteriorly at 4 h, 24 h and, in the above five patients, at 48 h. In some cases, spot scans of localized areas of activity were also taken at these times. If liver deposits were suspected, ^{99}Tc^{m} colloid subtraction imaging was performed in addition to the above procedures at either 4 h or 24 h. In three patients (Cases 1–3) blood samples were taken immediately after injection and at 1 h, 2 h, 4 h, 24 h and 48 h, and plasma radioactivity calculated as a percentage of injected activity per litre of blood.

Side-effects

The only side-effect noticed was in some of the earlier patients in which the counterion exchange procedure had not been carried out on the bisMSH-DTPA. It consisted of hypotension accompanied by flushing and was abolished when the peptide was infused in a large volume over a period of 20 min rather than being injected as a bolus. This problem was not apparent when trifluoroacetate was exchanged for acetate. No skin darkening was observed.

Scans were reviewed blind and the extent of metastatic disease assessed. These data were later correlated with X-ray computerized tomography (CT) and/or ultrasound investigations and the subsequent clinical progress of the patient. Organ and tumour uptakes were calculated from the scans and the distribution of radiation doses calculated.

Results

Clearance and organ distribution

Radioactivity was cleared rapidly from the plasma. The plasma concentration had reached 16.9% of the injected activity per litre, equivalent to a total plasma concentration of around 76%, within 15 min of the end of the infusion. The concentration fell rapidly thereafter reaching 2.84%/litre (total plasma ~ 13%) by 4 h and 0.81 %/litre (total ~ 3.6%) by 48 h (Fig. 1). Whole-body levels also fell rapidly, reaching 62.7±2.4% (SEM) of their initial values by 4 h, 45.0±1.9% (SEM) by 24 h and declining slowly thereafter (Fig. 2). Significant accumulation was noted in the kidney and liver. Uptake was highest in the kidneys and

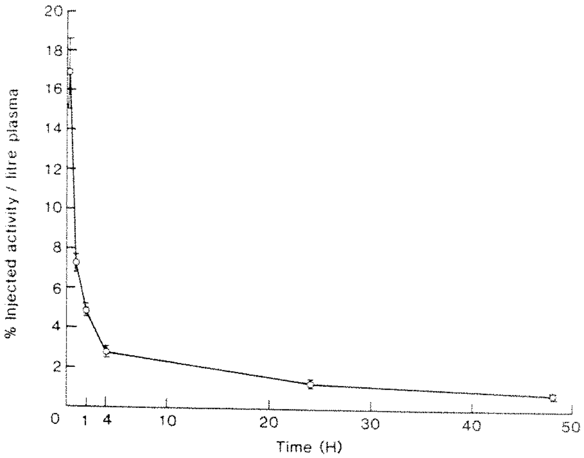

Figure 1. Clearance of ^{111}In-bisMSH-DTPA from plasma in human patients following a single injection. Mean values derived for Cases 1, 2 and 3±SEM (n = 3).

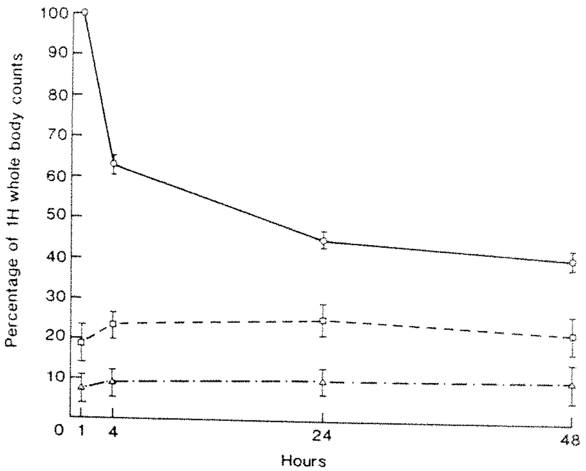

Figure 2. Whole-body, liver and kidney clearance of ^{111}In-bisMSH-DTPA. Results are expressed as the percentage of the 1 h whole-body counts±SEM, n = 3 (1 h kidney and liver), n = 5 (48 h liver, kidney and whole body), n = 9 (4 h and 24 h kidney and liver) or n = 13 (1 h, 4 h and 24 h whole body). Whole body, ○; kidney, □; liver, △.

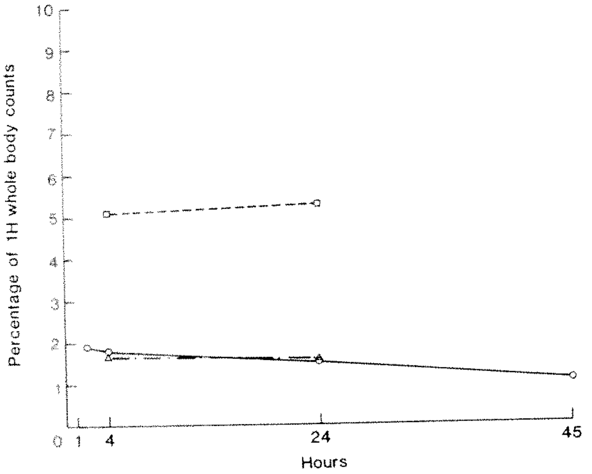

Figure 3. Tumour levels of ^{111}In-bisMSH-DTPA in man. Results are expressed as the percentage of 1 h whole-body counts uncorrected for tumour size for each of three patients. (○) Case 1; (□) Case 11; (△) Case 13.

accounted for up to 25% of the initial whole-body radioactivity at 24 h. Liver uptake was around 10% (Fig. 2). These figures did not change significantly between 4 and 48 h. Detailed pharmacokinetic and dosimetric calculations were performed on Cases 1 and 2 according to MIRD criteria (Snyder et al, 1975). The critical organ was the kidney, which received doses of 4.46 and 6.95 cGY in Cases 1 and 2, respectively. Doses to the liver were 1.04 and 0.59 cGy and non-specific doses to the rest of the body, including gonads, were 0.25 and 0.16 cGy. The whole-body effective dose equivalents were 6.6 and 6.9 mSv.

Tumour uptake

It was possible to measure tumour uptake quantitatively in three of the patients. Tumour uptake measured at 4 h was 1%, 5% and 1% of the 1 h whole-body counts in Cases 1, 11 and 13, respectively. In all of these patients, levels of radioactivity in the tumours remained virtually constant between 4 and 48 h (Fig. 3). In Case 1 an estimate of tumour size was possible, leading to a total tumour dose of 6.23 cGy.

Imaging of tumours

Known sites of disease could be clearly differentiated from the background radioactivity in nine patients (Cases 1, 4, 5, 6, 8, 10, 11, 12 and 13). In all these patients, tumour radioactivity had become sufficiently differentiated from the background to permit imaging within 4 h of injection. It was possible to continue imaging for at least 48 h, although no significant improvement in resolution was obtained in the later scans. All patients showed uptake associated with liver and kidney and, in some cases, non-specific bowel radioactivity could also be discerned. There was very little radioactivity associated with bone marrow or the central nervous system. Consequently, the best results were obtained with tumours located away from the liver, kidney and lower abdominal area.

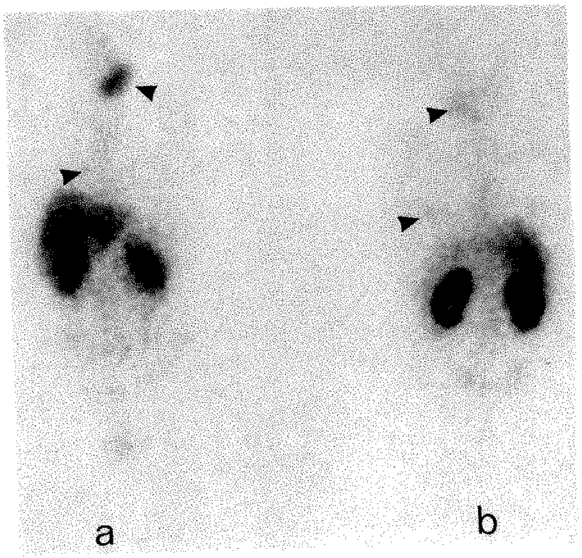

Figure 4. Whole-body scan of Case 1 taken 48 h after infusion of 40 MBq, 0.5 mg ^{111}In-bisMSH-DTPA showing normal uptake in liver and kidneys. Increased uptake is seen in a large lymph node metastasis in the left cervical region and small deposits are also visualized in the lung fields (arrowed). (a) Anterior, (b) posterior.

Figure 4 shows a 48 h whole-body scan of Case 1. This 54-year-old man was suffering from a large left submandibular mass, which had developed 4 years after the removal of a primary tumour from the left eyelid. Despite a normal chest radiograph, two unexpected deposits were discovered in the lungs, one in the right middle lobe and the other in the left lower lobe. Tumour activity at these sites was confirmed by the subsequent clinical progress of the patient.

Case 4, a 72-year-old man, had recurrent melanoma of the hard palate. The known deposit was imaged as well as a number of unsuspected metastases in the spine (Fig. 5), anterior mediastinum, right lung field and left sacro-iliac region.

Case 5 was a 59-year-old woman with recurrent melanoma in the left inguinal region and left iliac fossa. BisMSH-DTPA scanning demonstrated melanoma deposits in the left femoral, inguinal and para-aortic regions. The previously unsuspected abdominal metastases were confirmed by X-ray CT.

Case 6, a woman of 44 years, had multiple recurrent skin nodules of melanoma. BisMSH-DTPA scanning also showed uptake in a left supraclavicular node, the anterior mediastinum and right axilla.

Case 8, also a 44-year-old woman, had suspected liver metastases. Whilst these could not be distinguished from background on initial scanning, four deposits became clearly visible using the technetium colloid subtraction

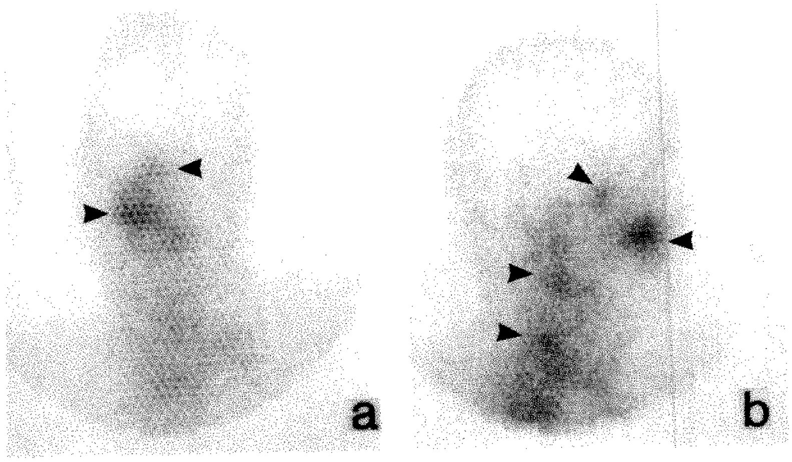

Figure 5. Scan showing the head and neck of Case 4, 4 h after infusion of 40 MBq, 0.5 mg ^{111}In-bisMSH-DTPA. Increased uptake is visible in the palate and skeletal deposits in the cervical spine. The lesion in the palate was the only one confirmed at the time of the scan. (a) Anterior, (b) right lateral.

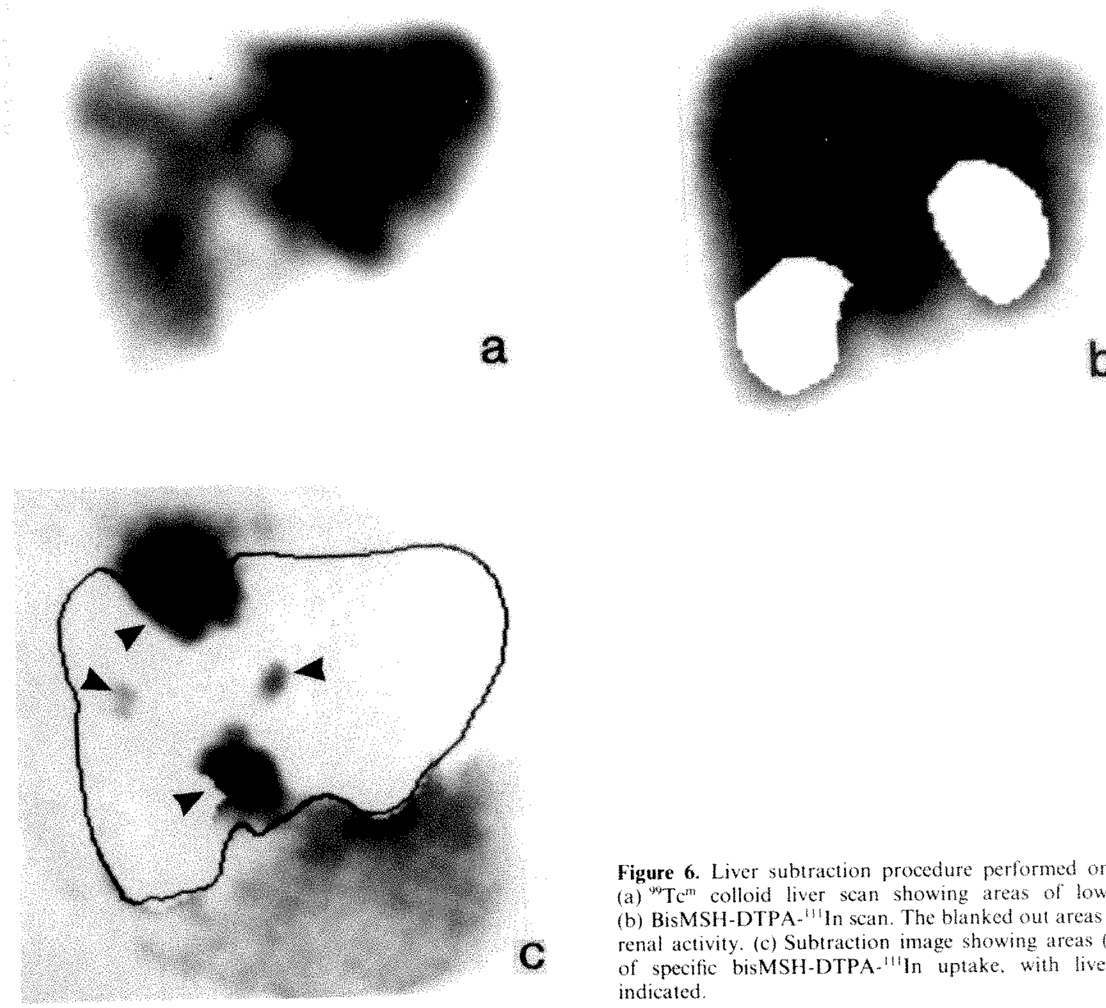

Figure 6. Liver subtraction procedure performed on Case 8. (a) ^{99}Tc^{m} colloid liver scan showing areas of low uptake. (b) BisMSH-DTPA-^{111}In scan. The blanked out areas represent renal activity. (c) Subtraction image showing areas (arrowed) of specific bisMSH-DTPA-^{111}In uptake, with liver outline indicated.

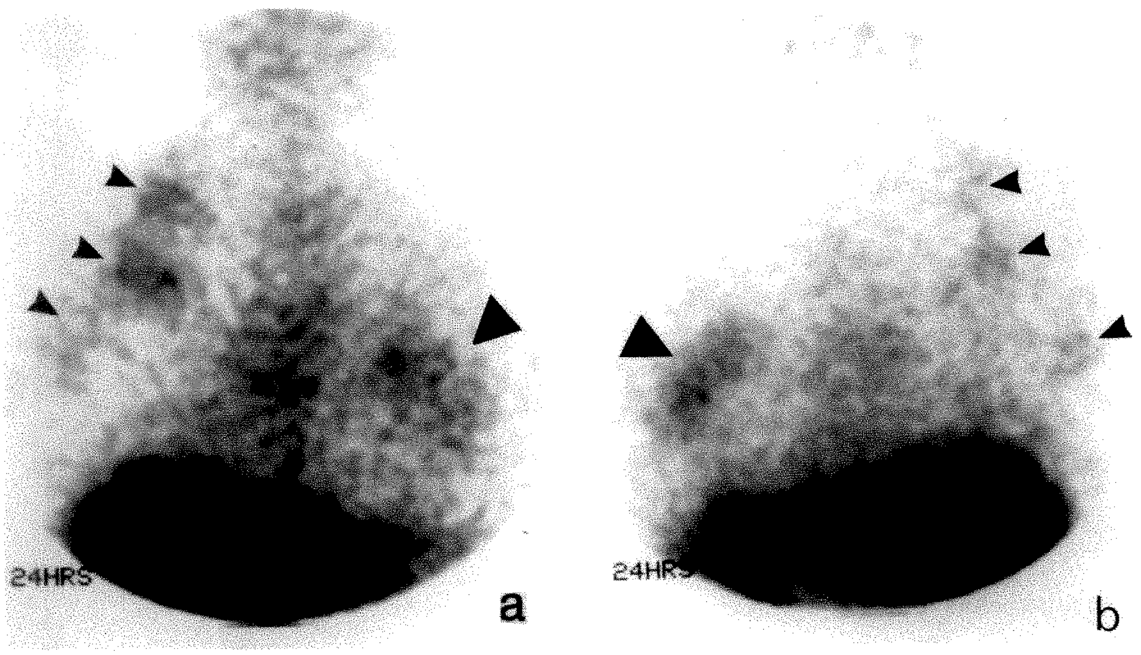

Figure 7. *Case 11*. (a) Anterior and (b) posterior scans of the thoracic area taken 24 h after injection of bisMSH-DTPA-^{111}In. Two lesions are visible in the right axilla and one in the supraclavicular region. There is also a further, previously unsuspected tumour visible in the left posterior chest (large arrowhead).

technique (Fig. 6). This patient also had two 20 mm lumps in the right breast and an involved lymph node in the left axilla, which were not imaged.

Case 10 was a woman of 51 years. Two nodules within a 150 mm × 100 mm diffusely infiltrated area on the left thigh and a 30 mm deposit in a left femoral node were successfully imaged. This patient subsequently showed a temporary spontaneous regression of the tumour. The tumour has since recurred.

In Case 11, a 34-year-old man, known deposits in the right axilla and supraclavicular region were imaged together with a second axillary metastasis and a further tumour in the left posterior chest, which has not previously been identified (Fig. 7).

Known deposits in the right foot and right axilla were identified in Case 12, a man of 22 years.

In Case 13, a man of 51 years, known lesions in the right shoulder (1), anterior mediastinum (3) and right posterior triangle of the neck (1) were identified. Scattered macules on the scalp (approx. 2 mm in diameter) and a 20 mm mass in the testis were not visualized.

Patients with negative scans

Cases 2 and 15 were originally referred with ultrasound diagnoses of liver metastases. These were not confirmed by other means and the patients have remained well for 18 months (Case 2) and 7 months (Case 15) after the date of the scan. Case 3, who was referred after excision of a primary nodule over the sternum, showed no active disease for 11 months. Case 7, who was scanned after block dissection of the right axilla, had no active disease eight months later. Case 9, who had had tumour excised from the left groin a month before the scan, did not develop any further disease for 7 months after scanning, and Case 14, who had had a primary nodule on the right ankle removed plus a right inguinal block dissection, remained disease free 3 months after the scan.

These data are summarized in Table I. They indicate that of a total of 46 positively identified lesions 10 mm or more in diameter, 41 (89%) were imaged with bisMSH-DTPA. Whilst the method did not image smaller tumours, the six patients with a completely negative scan were clinically clear of the disease at the time of the scan and in two (Cases 2 and 15) the method was instrumental in reversing a previous diagnosis based on ultrasound.

Discussion

The results indicate that bisMSH-DTPA is capable of imaging human melanomas with a high degree of accuracy. In all the patients with confirmed tumours, clear images were obtainable within 4 h of injection of the ^{111}In-bisMSH-DTPA complex. The rapidity of imaging indicates that the method might be improved further by the use of ^{99}Tc^{m} rather than ^{111}In. The gamma emission energy of ^{99}Tc^{m} (143 keV) is more suited to the detection characteristics of the gamma camera than those of ^{111}In (173, 247 keV). DTPA is not, however, an efficient chelator for technetium and an alternative, such as a

Table I. Detection of melanoma metastases greater than 10 mm in diameter in 15 patients using ^{111}In-bisMSH-DTPA

Case	Sex	Age	True positives	True negatives	False negatives
1	M	54	3	0	0
2	F	63	0	1	0
3	F	30	0	1	0
4	M	72	7	0	0
5	F	59	5	0	0
6	F	44	8	0	0
7	F	20	0	1	0
8	M	44	4	0	3
9	F	69	0	1	0
10	F	51	3	0	0
11	M	34	4	0	0
12	M	22	2	0	0
13	M	51	5	0	2
14	M	29	0	1	0
15	F	53	0	1	0
Total			41	6	5

89% of all lesions greater than 10 mm in diameter were detected. There were no false positives. No lesions under 10 mm were detected. Average age of patients (years) = 46, max. = 72, min. = 20.

diaminedithiol derivative (Fritzberg et al, 1988; Baidoo et al, 1990), would have to be used.

The only side-effect noted was a brief hypotensive episode in three patients, almost certainly due to the presence of trace quantities of trifluoroacetate present as a counterion associated with the peptide. The effect was completely abolished when this was replaced with acetate. In a clinical trial of MSH as a potential treatment for amenorrhoea, Kastin et al (1968) showed that repeated dosage of patients with 10 mg native MSH produced no marked side-effects other than a mild skin darkening. The absence of skin darkening in the present study is attributable to the low level of MSH dosage. Repeated daily injections of 20 mg MSH for an extended period are normally required to elicit a pronounced effect in man (Lerner et al, 1954).

A number of studies have shown either an inhibition of the growth of malignant melanocytes in the presence of MSH or no detectable effect (Eberle, 1988b) and hence it is unlikely that bisMSH-DTPA, especially at the dose used, has any adverse effect on the subsequent development of the tumour. None of the patients showed any detectable acceleration in growth of the tumour and indeed one, Case 10, experienced a temporary spontaneous regression.

A recent report suggests that receptors for MSH may not be present on all human melanomas (Tatro et al, 1990). We failed to image lesions over 10 mm in two patients (Cases 8 and 13). Tumours could, however, be detected at other sites in both patients. If this observation is attributable to a low level of receptor expression in the non-imaging lesions, it would imply that receptor expression can vary considerably within an individual patient. We were unable to examine any amelanotic lesions in the present study. Laboratory studies indicate, however, that loss of ability to synthesize melanin is due to a specific mutation in the gene coding for tyrosinase (Jackson & Bennett, 1990) and that amelanotic melanoma variants are not necessarily receptor deficient (Pawelek et al, 1975). There is therefore reason to suppose that it would be possible to image amelanotic as well as melanotic lesions with bisMSH-DTPA.

The question inevitably arises as to whether it would be possible to use MSH-based targeting to deliver therapeutic radionuclides or cytotoxic agents specifically to melanomas. Whereas the pharmacodynamic data suggest that useful amounts of a cytotoxic agent could be delivered to the tumour, the high concentrations seen in the liver and kidney would preclude bisMSH-DTPA being used, say, with yttrium 90 for therapy. Short-chain analogues of MSH with considerably enhanced hormonal activity have been described (Al Obeidi et al, 1989). Preliminary results obtained in tumour-bearing mice with a DTPA derivative of one of these suggests that much higher tumour/blood and tumour/liver ratios can be obtained (Bard et al, 1990b). Investigations using compounds of this type are currently in progress.

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Measurement of tibial torsion—a new technique applicable to ultrasound and computed tomography

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Abstract. A new method for measuring tibial torsion is described which can be applied to both ultrasound (US) and computed tomography (CT). The method has been validated in dry tibiae by comparison with direct measurements and with Jend's established CT method. In clinical practice a good statistical level of agreement has been demonstrated between the values obtained from US and CT scans. Both compared well with values obtained using Jend's CT technique. The use of US avoids exposure to radiation and is therefore suited to studying young subjects and controls and making repeat measurements.

Severe torsional abnormalities of the lower limb require the site and magnitude of the deformity to be determined accurately before corrective surgery. Smaller degrees of torsional malalignment of the lower limb may be important in the aetiology of conditions such as chondromalacia patellae. Therefore, it is necessary to have an accurate and reproducible method for measuring both femoral and tibial torsion.

Tibial torsion is defined as the angle between the transverse axes of the proximal and distal tibial articular surfaces. Several methods of measurement have been described using different anatomical landmarks to define the transverse axes and consequently a great variation has arisen in the values obtained. The current "gold standard" technique (Jend et al, 1981) is solely dependent on tibial landmarks and therefore measures true tibial rather than tibio-fibular torsion. The landmarks used in this technique require that full cross-sectional images of the tibia are obtained and, therefore, this technique has only been used with computed tomography (CT).

The aim of this study was to develop a method which was solely based on tibial landmarks but which could be applied to both CT and ultrasound (US).

Materials and methods

Two studies were undertaken. The first was on cadaveric dry tibiae and the second on patients with anterior knee pain syndrome attending a specialist knee clinic. Torsion was firstly measured in 21 dry tibiae by:

1. Jend's CT method (Fig. 1);
2. New method (Fig. 2); (a) from photographic images (direct measurement), (b) from CT scans, (c) from US scans.

Investigation of 21 patients with anterior knee pain syndrome (42 tibiae) was undertaken using both CT and US. Torsion was measured by:

1. Jend's CT method;
2. New method; (a) from CT scans, (b) from US scans.

In all cases the angle of torsion was calculated twice for each method from each set of scans. The values recorded in the results section are the means of these two measurements. In addition, two sets of US scans were obtained for the dry tibiae, allowing the repeatability of the new method to be assessed.

Direct measurements

The dry tibiae were placed supine on a horizontal surface resting on the posterior surface of the tibial plateau (the proximal tibial transverse axis) and the postero-lateral aspect of the distal tibia. A photographic image of the distal tibial articular surface was obtained (Fig. 3). The camera was positioned with the centre of the lens at the same vertical height as the centre of the distal articular surface and perpendicular to the long axis of the bone. The angle of torsion was then measured between the distal transverse axis (as defined by our new method) and the horizontal.

US method

The dry tibiae and the patients were scanned using similar techniques although a silicon gel "stand-off" was needed to scan the dry bones in the absence of any soft tissues. A static image B-mode ultrasound scanner was used (Philips Rohnar 5550) fitted with a 6 mm diameter 5 MHz transducer. Although it is technically easier to use a static image B-mode scanner, it is possible to use a

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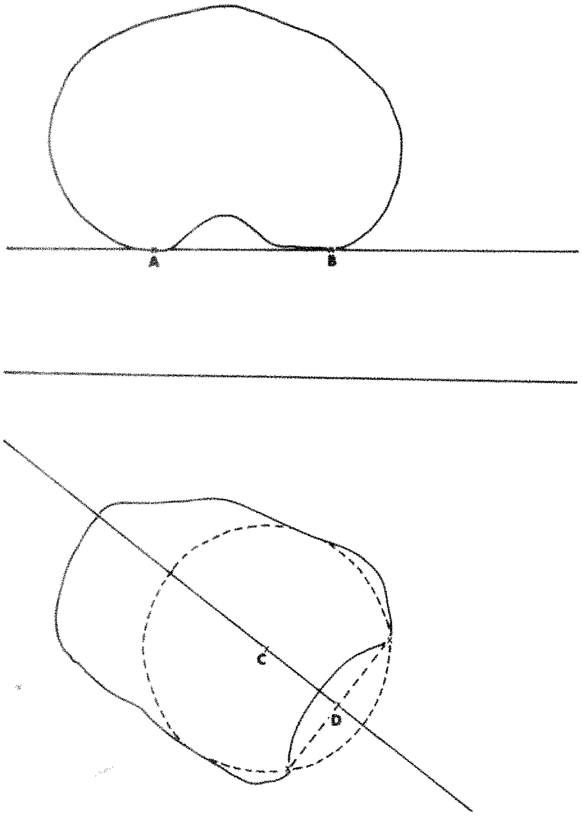


Figure 1. Jend's CT method. The proximal axis is a line joining the most posterior points of the tibial condyles (A–B). The distal axis lies between the centrepoint of a circle that fits into the cross-sectional image of the tibia, including the defect of the fibular notch and excluding the bulge of the medial malleolus (the "pilon centrepoint"), and the midpoint of a line drawn across the fibular notch (C–D).

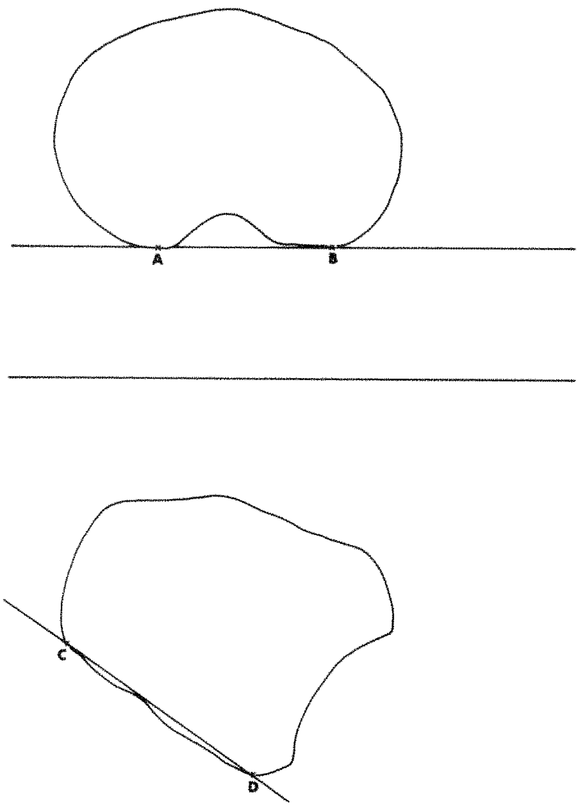


Figure 2. New method. The proximal axis is as for Jend's technique (A–B). The distal axis (C–D) lies between the two points on the posterior tibial border at which this border sweeps sharply anteriorly to join the medial malleolus and the lateral tibial border. These landmarks were easily identified on all the bones studied.

real-time scanner provided that the probe is held vertically at all times (Joseph et al, 1987; Upadhyay et al, 1987). The tibiae were secured to an ordinary examination table to prevent any movement during the examination and were scanned prone. The proximal scans were obtained at the level of tibial plateau parallel and immediately distal to the articular surface. In the patient group the upper border of the fibular head provided a reliable landmark. The probe was gently moved over the posterior surface of the leg from one midlateral point to the other, until the posterior surface of the proximal tibia could be seen as a continuous line on the monitor. The distal scans were obtained at the level of the base rather than at the tip of the medial malleolus so that the fibular notch was included. The probe was passed from a position just anterior to the medial malleolus, over the surface of the medial malleolus, over the long flexor and achilles tendons and finally over the surface of the lateral malleolus until the whole of the posterior tibial border was visualized on the monitor screen. Both the

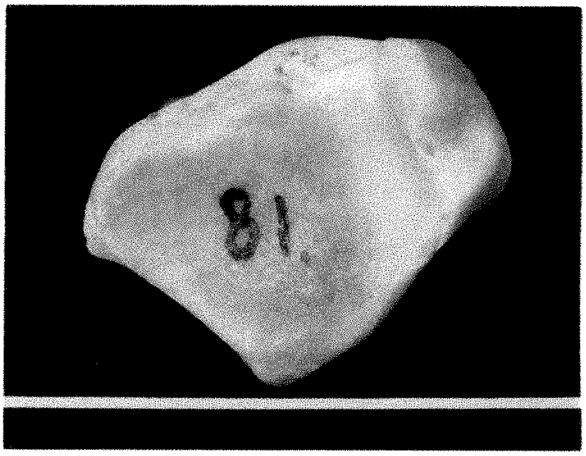
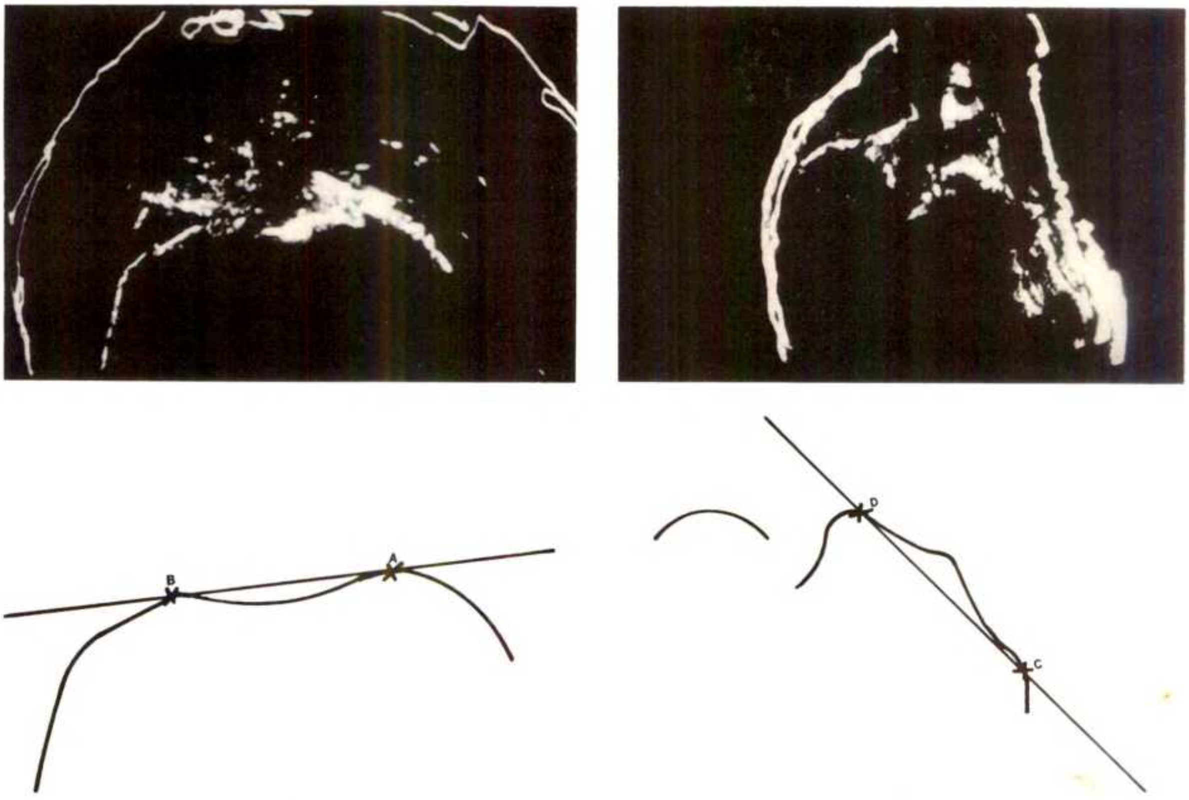


Figure 3. Photographic image of the distal articular surface of a right tibia used to obtain a direct measurement of the angle of torsion.



(a) (b)

Figure 4. US scans of a patient's left tibia with accompanying line drawings demonstrating the bony landmarks used to determine the proximal (a) and distal (b) transverse axes for the new method.

proximal and distal scans were recorded on polaroid film (Fig. 4a & b).

CT method

The dry bones and patients were both scanned using a similar CT technique. The scans were performed using a Siemens Somatom DRH scanner with the dry tibiae positioned as described for the direct measurements. The patients were scanned lying supine. In all instances the tibiae were firmly secured to the examination table and a topogram was obtained to select the desired levels for imaging. Slices with a 4 mm thickness were then taken (a) through the tibial plateau and (b) immediately proximal to the horizontal part of the distal tibial articular surface. The images were recorded on radiographic film (Fig. 5a & b).

Calculating the angle of torsion

The angle of torsion was calculated by making a tracing of the bony landmarks from the distal image and then superimposing the landmarks from the proximal image onto the tracing, ensuring that the relationship of each image to the horizontal was maintained. This was done by marking the corners of the images onto the tracing. The proximal and distal axes were then drawn on the tracing and the angle of torsion was measured with a protractor.

Results

Dry tibiae (Tables I, II & III)

The direct measurements, the US and CT measurements derived from the new method all gave similar mean values and standard deviations (SD). The mean values obtained using the new method were slightly lower than using Jend's method. There was also a left/right difference with the right tibia having greater external torsion whichever method of measurement was used. This varied from 0.4° difference on the direct measurements to 3.2° difference using Jend's technique.

The correlation between the various methods can be demonstrated either diagrammatically (Fig. 6) or by calculating correlation coefficients. However, the level of agreement between two methods of measurement has been shown to be best demonstrated by calculating the differences between the means (dM) and the standard deviations of the differences (SDd) for each set of values (Bland & Altman, 1986).

The difference between the means represents the bias

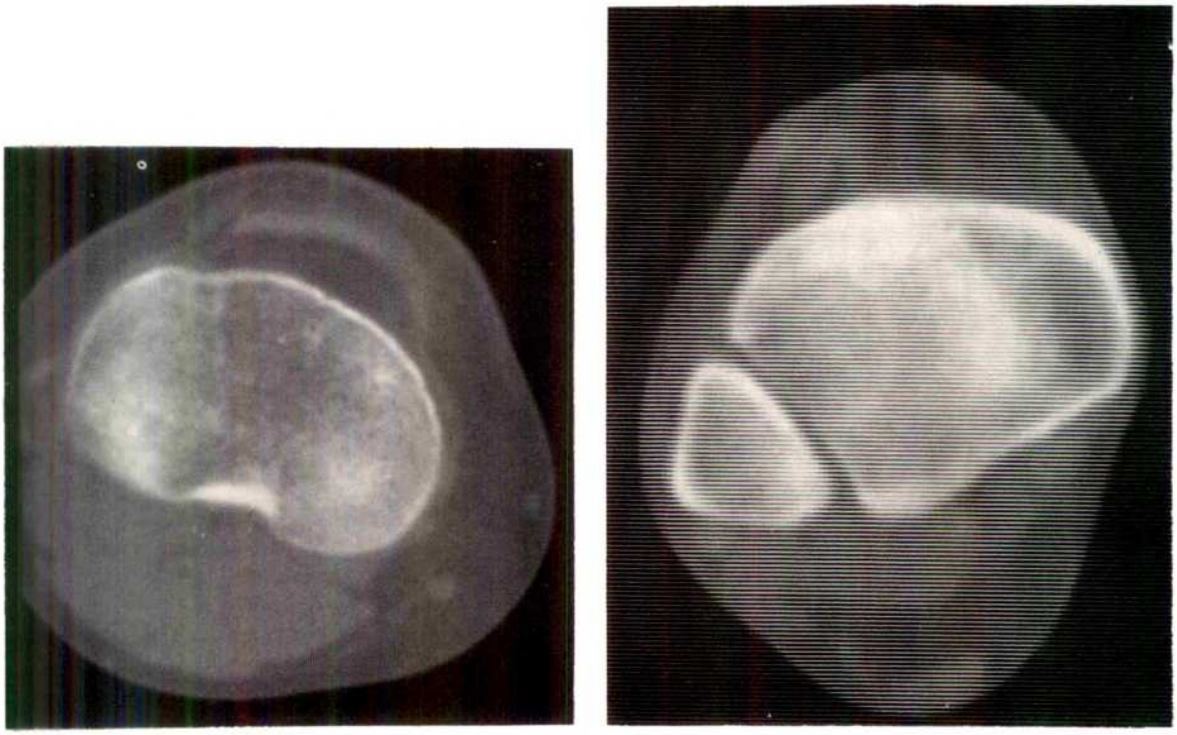

(a) (b)

Figure 5. CT scans of a patient's right tibia demonstrating the bony landmarks used to determine the proximal (a) and distal (b) transverse axes for the new method.

Table I. Dry tibiae. Tibial torsion measurements (degrees). These values were obtained from direct measurements, US and CT scans for the new method and from CT scans using Jend's method. The values in the table are the averages of two measurements made on each set of images. Two sets of US scans were performed

Tibia	Side	Direct	US 1	US 2	CT	CT Jend
01	L	40.0	39.0	39.0	39.0	44.5
02	L	34.5	32.0	35.5	32.5	33.5
03	L	40.5	45.0	43.5	42.0	43.0
04	R	28.0	27.5	25.0	25.5	31.0
05	L	40.0	37.5	38.5	36.0	44.5
06	R	40.5	44.0	43.0	40.5	48.5
07	L	37.0	40.5	40.5	33.5	33.5
08	R	43.0	45.0	44.0	44.5	51.5
09	R	47.0	52.0	53.0	50.0	55.5
10	R	47.0	50.0	50.0	48.0	52.5
11	R	42.0	43.5	38.0	42.0	44.5
12	R	31.5	28.5	30.5	29.0	25.5
13	L	37.0	37.5	35.0	33.0	35.5
14	R	27.5	31.5	29.5	30.5	34.0
15	L	30.0	34.0	31.5	31.0	32.5
16	R	32.5	33.0	35.5	34.0	42.5
17	R	40.0	41.0	41.5	39.5	47.0
18	R	32.5	33.0	35.0	33.5	34.0
19	L	29.0	30.0	31.0	31.0	33.0
20	L	36.5	37.5	36.0	37.0	42.5
21	R	26.0	26.0	25.0	27.5	28.5

Table II. Dry tibiae. Mean values and standard deviations (SD) for tibial torsion measured by the various methods. The overall results for the 21 tibiae are shown as well as the results for the nine left and 12 right tibiae

	Direct	US 1	US 2	CT	CT Jend
Mean (SD) all	36.3 (6.3)	37.5 (7.3)	37.2 (7.3)	36.2 (6.6)	39.9 (8.5)
Mean (SD) left	36.1 (4.2)	37.0 (4.5)	36.7 (4.1)	35.0 (3.8)	38.1 (5.4)
Mean (SD) right	36.5 (7.6)	37.9 (9.0)	37.5 (9.2)	37.0 (8.2)	41.3 (10.2)

Table III. Dry tibiae. Agreement between different methods expressed as the difference between the means (dM) and the standard deviations of the differences (SDd). The 95% confidence limits for the methods being compared are also shown (dM + 2 × SD). The mean of both sets of US values has been used in these calculations

Methods compared	dM	SDd	95% confidence limits
US *vs.* direct	+1.06°	±2.17°	+1.06±4.34°
CT *vs.* direct	−0.12°	±2.19°	−0.12±4.38°
US *vs.* CT Jend	−2.54°	±3.82°	−2.54±7.64°
CT *vs.* CT Jend	−3.71°	±3.25°	−3.71±6.50°
US *vs.* CT	+1.18°	±1.92°	+1.18±3.84°
US (1) *vs.* US (2)	+0.36°	±2.09°	+0.36±4.18°

between the two methods and the 95% confidence limits for agreement can easily be determined by doubling the SDd and adding this to the bias (Table III). It can therefore be seen that there was an excellent level of agreement between the new CT method and the direct measurements; between the new US method and the direct measurements; between the new CT and US methods, and between the two sets of US measurements.

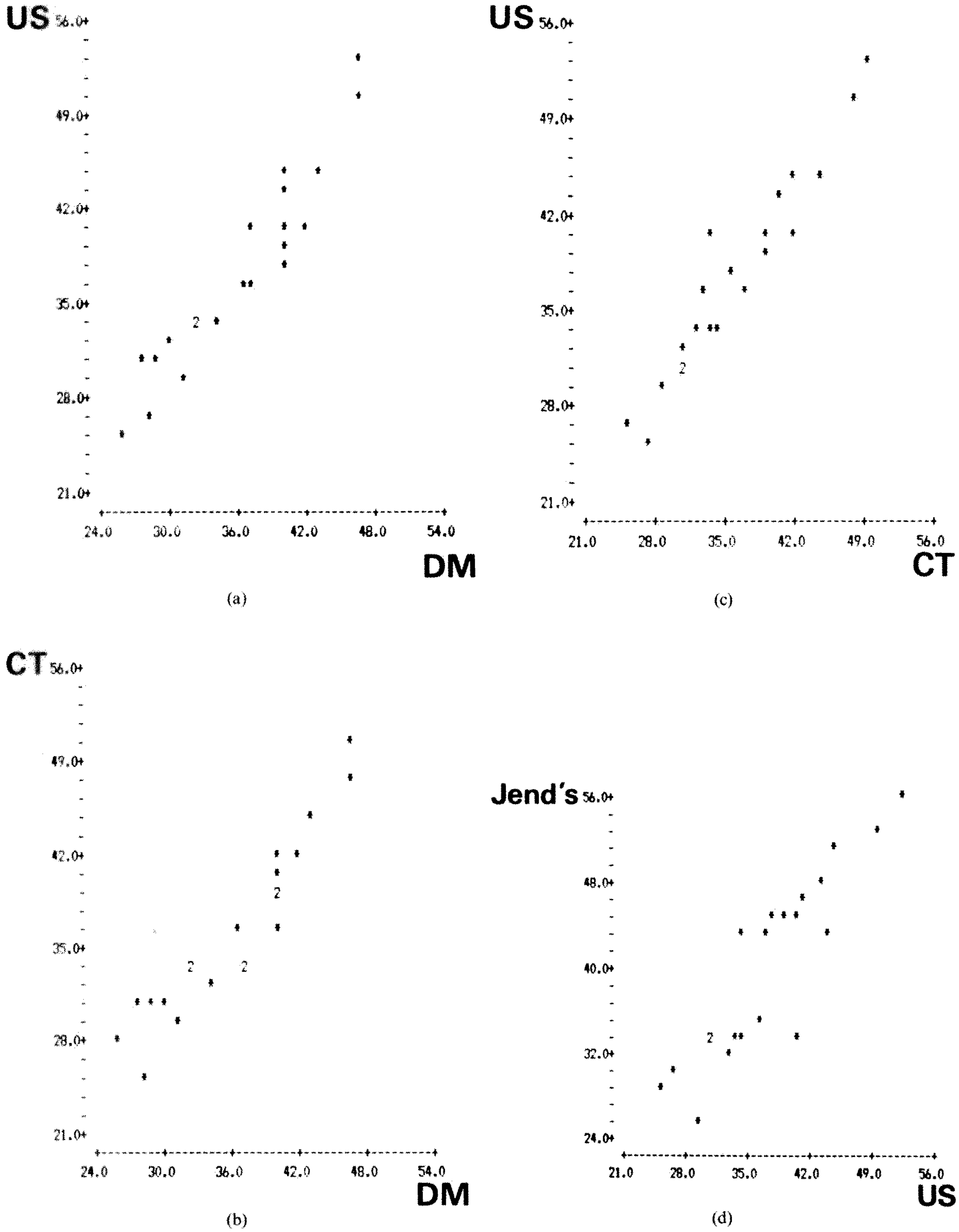
The level of agreement between the values obtained using the new method and those obtained using Jend's method were not quite as good. The bias was small (−2.54° for US and −3.71 for CT) but the 95% confidence limits were greater as different landmarks were used.

Patients (Tables IV, V, VI)

The differences between the values for torsion obtained by the new CT and US methods were very small indeed. Differences between the values obtained by the new method and by Jend's CT method were smaller than in the dry tibiae group. The values were generally higher with a greater variation from the mean than for the dry tibiae. As in the dry tibiae group, there was a left/right difference, with the right tibia having greater external torsion whichever method of measure-

Table IV. Patients. Tibial torsion measurements (degrees). The values shown are the averages of two measurements made on each set of scans. Measurements were obtained from US and CT scans for the new method and from CT scans for Jend's method

Patient	Sex	Left tibia			Right tibia		
		US	CT	CT Jend	US	CT	CT Jend
01	M	41.0	40.0	39.0	42.0	42.0	38.0
02	M	30.0	29.0	24.0	30.5	28.0	27.5
03	M	30.0	29.5	25.5	36.5	39.0	34.0
04	M	42.5	38.5	37.0	51.0	50.0	49.5
05	F	51.0	54.0	53.0	56.0	58.0	58.5
06	F	31.5	31.0	39.0	31.5	31.0	37.5
07	F	49.5	44.5	47.0	51.5	44.5	47.5
08	F	48.0	49.0	49.0	54.5	55.0	56.0
09	F	46.0	41.0	42.5	37.5	35.5	39.5
10	F	42.5	43.0	47.5	53.0	49.0	56.0
11	F	33.0	36.0	40.0	43.5	46.0	49.5
12	F	56.5	50.0	56.0	63.5	57.0	67.0
13	F	24.5	23.0	26.5	23.5	23.5	28.0
14	F	62.5	55.5	61.5	65.0	58.0	62.0
15	F	47.0	42.0	43.0	48.0	44.0	43.5
16	F	38.0	40.0	39.5	48.5	45.5	46.0
17	F	32.0	33.5	35.5	35.0	39.0	36.0
18	F	37.0	38.0	43.0	36.0	33.0	41.5
19	F	51.5	51.5	49.0	60.5	56.5	58.0
20	F	38.5	39.5	38.5	45.0	39.0	38.5
21	F	29.0	28.0	32.5	54.0	49.5	59.5



(a)

(c)

(b)

(d)

Figure 6. Scatter graphs demonstrating the correlation between the torsional values obtained using the various methods of measurement in the dry tibiae. The new US and CT methods are plotted against the direct measurements (a, b); the US method is plotted against the new CT method (c) and Jend's CT method is plotted against the US method (d).

Table V. Patients. Mean values and standard deviations (SD) for tibial torsion measured by the various methods. The overall values are shown as well as the values for the left and for the right tibiae

	US	CT	CT Jend
Mean (SD) all	43.5 (10.9)	41.9 (9.7)	43.9 (10.7)
Mean (SD) left	41.0 (10.1)	39.8 (8.9)	41.4 (9.7)
Mean (SD) right	46.0 (11.4)	44.0 (10.1)	46.4 (11.3)

Table VI. Patients. Agreement between different methods expressed as the difference between the means (dM) and the standard deviations of the differences (SDd). The 95% confidence limits for the methods being compared are also shown (dM + 2 × SD)

Methods compared	dM	SDd	95% confidence limits
US *vs.* CT Jend	−0.33°	±3.98°	−0.33° ± 7.96°
CT *vs.* CT Jend	−1.96°	±3.91°	−1.96° ± 7.82°
US *vs.* CT	+1.63°	±3.16°	+1.63° ± 7.32°

ment was used. The difference was 4.2° for the new CT method and 5.0° for both the US and Jend's method.

The level of agreement between the new US and CT methods was almost as good as in the dry tibiae group, the US again giving slightly higher values. For a CT value of 40° the 95% confidence limits for the US value would be 41.63° ± 6.32°. The level of agreement between the new method and Jend's method was slightly better than that found in the dry bones: the difference between the means was smaller in the patient group, although the SDd were almost identical.

Discussion

Torsional deformities of the tibia have been reported to be associated with club foot (Wynne-Davies, 1964), patello-femoral instability (Ficat & Hungerford, 1977), Osgood-Schlatter's disease (Turner & Smillie, 1981) and medial compartment osteoarthritis (Yagi & Sasaki, 1986). However, the absence of an accurate, reliable, standardized technique for measuring tibial torsion has made interpretation of the significance of some of these reports difficult.

Several fundamentally different techniques have been used to measure tibial torsion such as calipers, tropometers, plain radiography, fluoroscopy, computed tomography (CT) and more recently ultrasound. CT has become the preferred technique (Jakob et al, 1980; Jend et al, 1981) as it allows detailed cross sectional images of the tibia to be obtained at the relevant levels enabling the transverse axes to be determined accurately. Nevertheless, some doubt concerning the reproducibility of various CT methods has been raised (Laasonen et al, 1984) and a perfect method has yet to be found.

In addition to the different investigative techniques already mentioned, different authors have used different methods for determining the proximal and distal transverse tibial axes. This has resulted in a huge variation in the reported normal ranges for tibial torsion. It is generally accepted that the posterior border of the tibial condyles constitutes an acceptable proximal reference line, but several distal tibial reference lines have been proposed. Methods using both malleoli as reference points include all the clinical and plain radiographic methods (Hutter & Scot, 1949; Rosen & Sandick, 1955; Wynne-Davies, 1964; Staheli & Engel, 1972; Turner & Smillie, 1981) and some CT methods (Jakob et al, 1980; Widjaja et al, 1985; Yagi & Sasaki, 1986). However, all these strictly measure tibio-fibular rather than tibial torsion.

In only two methods has the distal reference line been drawn from solely tibial landmarks (Jend et al, 1981; Joseph et al, 1987). Jend's CT method has been described already (Fig. 1) and can be regarded as the current "gold standard". Joseph et al (1987) used an ultrasound technique to measure tibial torsion in children which has been used only sparingly by other investigators (Krishna et al, 1991). The advantages of an ultrasound technique are obvious. It avoids exposure to radiation which is particularly important in younger patients, control groups and when repeated measurements are required. It is also relatively inexpensive compared with CT and can be performed in the orthopaedic laboratory.

It is perhaps surprising that these have been the only reports of the use of ultrasound for measuring tibial torsion, since ultrasound has been quite widely used to measure femoral anteversion (Upadhyay et al, 1987). There have been some recent reports (Berman et al, 1987; Lausten et al, 1989) suggesting that ultrasound is not sufficiently accurate to measure femoral anteversion clinically. This is because the femoral neck axis measured by ultrasound relies on drawing a line from the most anterior part of the greater trochanter to the most anterior part of the femoral head, which does not necessarily correlate with the true longitudinal axis of the femoral neck. No such problem is encountered when using ultrasound to measure tibial torsion, since the posterior tibial border can be used to determine both the proximal and distal tibial transverse axes.

The main reason that ultrasound has not been widely used to measure tibial torsion is that it is very difficult to obtain full cross sectional images of the tibia, and existing methods such as Jend's could not therefore be applied to it. In their study on children, Joseph et al (1987) used the posterior tibial border as the distal transverse axis. They found that it was sometimes difficult to draw this line when the posterior border was curved, but remarked that this only occurred rarely. Our experience in both adult dry tibiae and live adult patients is that the posterior border of the distal tibia is only rarely straight. We found this technique difficult to use for the majority of cases.

Using our method, we have found the landmarks on the posterior distal tibial border to be consistently identifiable, enabling the distal transverse axis to be determined accurately. Once the technique was mastered, no difficulty was encountered in measuring tibial torsion in any of the dry bones or patients studied. Similar values for tibial torsion were obtained whether direct measurements, CT or US were used, confirming the reliability of the imaging techniques. The repeatability of the US method was also very good as the difference between the means and the SDd were both very small (0.36° and ±2.09°, respectively). There was a left/right difference in both the dry bone and patient groups with all the methods used, with the right tibiae having greater external torsion than the left tibiae. This finding has been reported recently in a study of normal subjects (Clementz, 1988).

In summary, our method gives results which are comparable with those obtained using the present "gold standard" technique described by Jend, but it also combines the advantages of an ultrasound technique. This allows tibial torsion to be measured in the orthopaedic laboratory, at relatively low cost and without exposing patients or controls to radiation.

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Measurement of forearm bone mineral density in normal women by dual-energy X-ray absorptiometry

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Abstract. We report the results of forearm measurements, without the use of a water bath, using dual-energy X-ray absorptiometry (DEXA) in 100 normal women aged 29–69 years (average age, 52 years). Studies were performed using the Hologic QDR-1000, with bone mineral density (BMD) measured at three sites in the non-dominant forearm: ultradistal, distal one-third and a region between these two. The precision of the technique was 0.74%, 0.55% and 0.58%, respectively. The normal range for forearm BMD and variation with age was established. BMD was also measured in the lumbar spine (L1–L4) and femoral neck. Linear regression analysis gave a range of correlation coefficients between forearm and axial sites of $r = 0.49$–0.67. Standard errors of the estimate (SEE) in predicting axial from peripheral measurements gave average values from the three forearm sites of 0.085 g/cm^2 for the femoral neck and 0.118 g/cm^2 for the spine. Forearm measurements using DEXA can now be reliably performed in air. DEXA produces a high-resolution image, is fast and simple to perform, and enables both cortical and trabecular sites to be examined in one measurement. Forearm and axial measurements can be performed using the same equipment, where centres possess a suitable DEXA system.

Forearm bone density has for many years been measured by single-photon absorptiometry (SPA) (Cameron & Sorenson, 1963), but the clinical role of forearm measurements has been challenged following the introduction of quantitative computed tomography (QCT) and dual-photon absorptiometry (DPA). These techniques enable direct examination of trabecular bone of the axial skeleton (Mazess et al, 1984), where the most serious fractures, in terms of ill health and cost, occur (Melton & Riggs, 1983).

Measurement of forearm bone mineral density (BMD) remains valuable, however. It is a better discriminator of peripheral fracture than axial BMD in retrospective studies (Eastell et al, 1989), and when used for the diagnosis of osteoporosis, forearm BMD and vertebral BMD have given similar percentages of misclassified cases (Nordin et al, 1988). Also importantly, several prospective studies have found the risk of all types of fractures, including hip fracture, to be highest among women with the lowest bone mass in the radius (Hui et al, 1989; Gardsell et al, 1989; Cummings et al, 1990). Furthermore, there is prospective evidence that appendicular BMD is superior to spinal BMD for the prediction of spinal fracture, though this may be explained by the high prevalence of aortic calcification and osteophyte formation in the patients in the study whose mean age was 63.3 years (Wasnich et al, 1989).

Software is now available to measure forearm BMD with dual-energy X-ray absorptiometry (DEXA), which exposes the patient to less radiation than axial DEXA. The advantages over SPA include: (i) a high-resolution image that aids repositioning of regions; (ii) no need for a water bath; (iii) both cortical and trabecular sites can be examined in one measurement; and (iv) a radiation source (^{125}I for SPA) is not necessary (Sorenson & Cameron, 1967; Cameron et al, 1986). In this study we have examined forearm BMD measurements using DEXA on 100 normal women to determine a normal range and variation with age, precision and standard errors of estimates of axial from forearm BMD.

Methods

DEXA was performed in 100 women aged 29 to 69 years (average age 52 years) referred by general practitioners for measurement of BMD. Studies were undertaken with the Hologic QDR-1000 and each patient had scans of the non-dominant forearm, lumbar spine and left hip. The forearm measurement was obtained with the patient seated, the arm resting on the table and straight in relation to the table's long axis. The arm was resting against a foam block and held at about 105°. Scanning was begun halfway between the ulnar styloid and the olecranon. Using the manufacturer's software, BMD was calculated at three sites in the forearm: (i) an ultradistal region consisting of a 1.5 cm band adjacent to the end plate of the radius; (ii) a "one-third radius" region, a 2 cm wide band centred one-third of the distance between the ulnar styloid and the olecranon; and (iii) a larger mid-distal region comprising the rest of the distal forearm between these two sites. Lumbar spine BMD was averaged over L1–L4 and femoral neck BMD was measured in a 1.5 cm band adjacent to the greater trochanter. A typical forearm scan result is seen in Fig. 1.

All women referred over a period of 6 months for measurement of BMD by their general practitioners to

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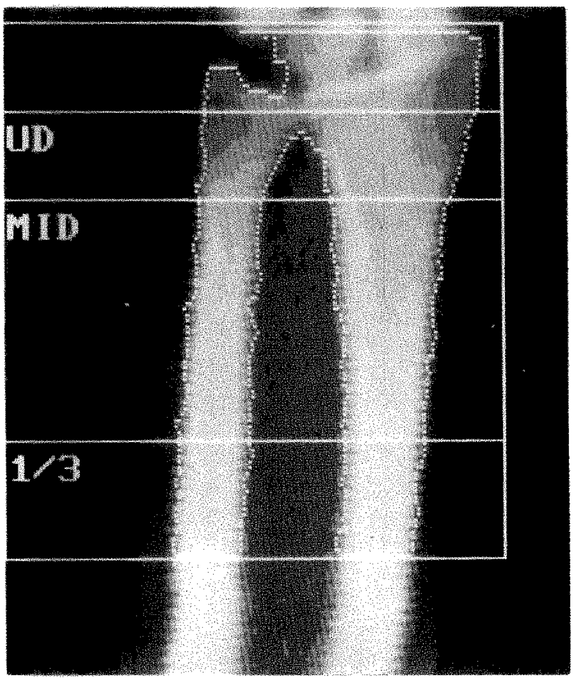

Figure 1. Images from the forearm using dual-energy X-ray absorptiometry, showing the three regions measured.

Table II. Linear regression correlation coefficients for BMD versus age

Site of BMD measurement	Correlation coefficient (r)	
Ultradistal forearm	−0.390	($p < 0.01$)
Mid forearm	−0.418	($p < 0.01$)
One-third radius	−0.431	($p < 0.01$)
Lumbar spine	−0.222	($p < 0.05$)
Femoral neck	−0.317	($p < 0.01$)

assess their risk of osteoporosis were eligible for inclusion. To obtain a "normal" population, women were excluded if there was known osteopenia or vertebral collapse before referral or a history of fractures. They were also excluded if they had a history of factors that might influence bone density and this information was obtained from a questionnaire completed with the assistance of a trained nurse when their bone density was measured. These factors included a menopause before age 40 years, hormone replacement therapy for more than a year, secondary amenorrhoea for more than 6 months, any use of corticosteroids and a history of chronic conditions such as thyrotoxicosis and anorexia nervosa.

The BMD measurements were used to construct a normal range for the forearm, to establish the variation with age and examine the correlation between forearm sites and BMD in the lumbar spine and hip. There was only a small number of women whose age was less than 40 years or more than 60 years and these were excluded from the construction of a normal range. Linear regression analysis was used to calculate the predictive value of forearm BMD for axial BMD in terms of the standard error of the estimate (SEE). The long-term stability of the QDR-1000 measurements was investigated over the time of the study with daily scans using a Hologic anthropomorphic spine phantom. Four studies over 2 weeks were undertaken in six normal volunteers to establish the *in vivo* precision of measurements from the non-dominant forearm, lumbar spine and femoral neck.

Results

An average BMD coefficient of variation of 0.74%, and 0.58% and 0.55% g/cm^2 was obtained for the ultradistal, mid-distal and one-third radius regions of the forearm, respectively. The precision values for the femoral neck were an average of 1.2% and for the lumbar spine an average of 1.1%. Tests of skewness and kurtosis were applied to all the bone density data and standardized coefficients all lay within the range −2.0 to +2.0, confirming normal distributions.

The results of the mean and standard deviation for forearm, spinal and femoral BMD against age are given in Table I with the results for linear regression of BMD against age in Table II. The forearm measurements are also displayed in Fig. 2. Over the age range 40–60 years there was a 15% fall in ultradistal BMD, 11% fall in mid-distal BMD and 10% fall in distal one-third BMD. Over the same period there was a 15% fall in lumbar spine BMD and a 13% fall in femoral neck BMD. We compared our results for the lumbar spine and femoral neck with the normal American data provided by Hologic, by calculating a ratio of Guy's/Hologic values for each age band. These were then averaged to produce a mean ratio for the spine and hip. Values obtained with 95% confidence limits for the spine were 0.990 ± 0.15 (not significant) and for the hip 0.961 ± 0.018

Table I. Mean and standard deviation of BMD (in g/cm^2) versus age

Age (years)	Numbers	Ultradistal forearm		Mid-distal forearm		One-third radius		Lumbar spine		Femoral neck	
		Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD
41–45	14	0.394	0.048	0.531	0.047	0.616	0.052	1.001	0.127	0.812	0.110
46–50	20	0.394	0.036	0.527	0.028	0.614	0.036	0.962	0.102	0.763	0.079
51–55	32	0.377	0.043	0.514	0.054	0.609	0.051	0.966	0.145	0.765	0.175
56–60	18	0.335	0.042	0.475	0.036	0.553	0.040	0.852	0.118	0.707	0.060

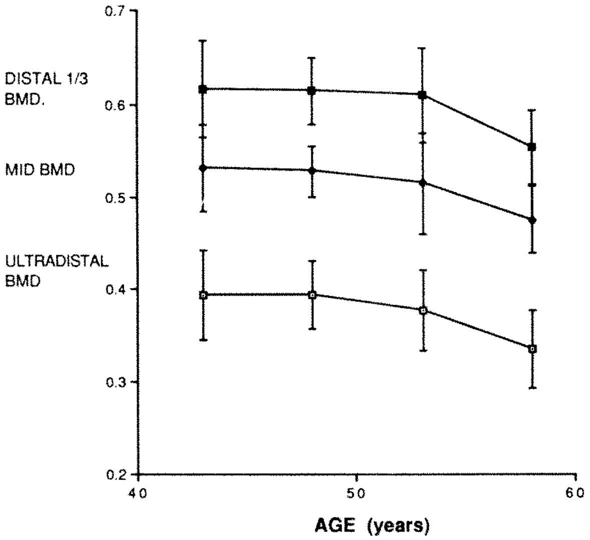

Figure 2. Forearm BMD (mean and standard deviation) versus age.

($p < 0.001$). Normal American Hologic data were unavailable for the forearm.

The correlation coefficients between BMD measured at the three forearm sites and between forearm and axial BMD are shown in Table III, together with SEEs for measurement of axial BMD from forearm BMD. The ultradistal radius gives the strongest correlation coefficients between a peripheral site and the axial sites, with $r = 0.67$ for the lumbar spine and $r = 0.57$ for the fermoral neck. The regression relationships of ultradistal to axial measurements are shown in Figs 3 and 4. There are significant correlations between all radial sites and these are greatest between adjacent positions.

Discussion

Our data on precision gives average values of 1.1% for the lumbar spine, 1.2% for the femoral neck, and forearm values of 0.74% or less. This is better than reported results for DPA at axial sites (3–6%) (Wilson & Matson, 1977), and compares favourably with most

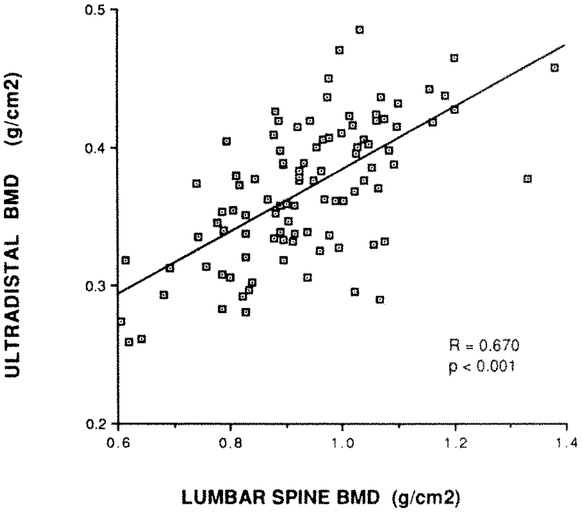

Figure 3. The relationship between ultradistal BMD and spinal BMD.

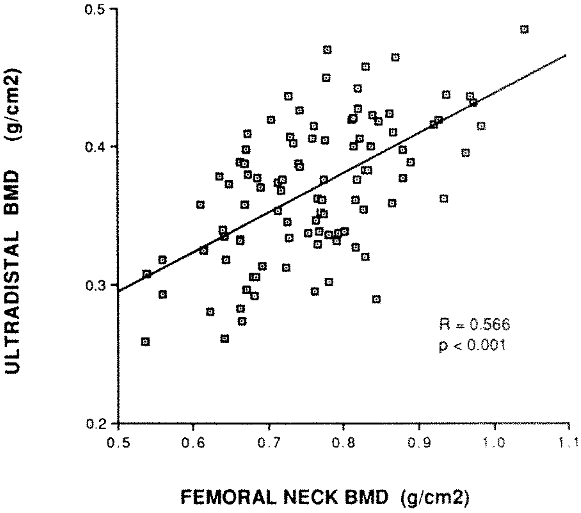

Figure 4. The relationship between ultradistal BMD and femoral neck BMD.

Table III. Correlation of BMD results between different sites, expressed as r values, and SEE for spinal and femoral BMD

Site	r	p	SEE
Ultradistal forearm v. lumbar spine	0.670	< 0.001	0.109
Ultradistal forearm v. femoral neck	0.566	< 0.001	0.084
Mid forearm v. lumbar spine	0.561	< 0.001	0.120
Mid forearm v. femoral neck	0.554	< 0.001	0.085
One-third radius v. lumbar spine	0.532	< 0.001	0.124
One-third radius v. femoral neck	0.491	< 0.001	0.086
Ultradistal forearm v. mid forearm	0.800	< 0.001	—
Ultradistal forearm v. one-third radius	0.630	< 0.001	—
Mid forearm v. one-third radius	0.888	< 0.001	—

studies of SPA at peripheral sites, which give precision values of 2–5% (Riggs et al, 1981; Johnston, 1983), though some centres have reported values as low as 1–1.5% (Nilas et al, 1985).

The mean spinal and femoral neck BMDs are close to those of the American Hologic normal range and the same as found for a larger group of 468 normal women over the same age range, confirming that the 100 women in this study reflect a normal British population (Ryan et al, 1990). The mean values for forearm and axial BMD do not show a significant fall with age until age 56–60 years. These forearm results are similar to those found in most studies using SPA (Guesens et al, 1985; Bilbrey et al, 1988), and axial results are similar to a previous study of British women using DEXA (Hall et al, 1990). There is a greater fall in ultradistal BMD (15%) from age 40–60 years than at other forearm sites (11% mid-distal, 10% one-third radius). Ultradistal bone mass is mostly trabecular bone whereas mid-distal is a mixture of cortical and trabecular bone and the one-third radius region is largely cortical bone (Hologic users manual; Schlenker & Von Seggen, 1976; Nilas et al, 1987; Eastell et al, 1989). This supports the view that trabecular bone is more sensitive than cortical bone to the main causes of bone loss over this period, largely due to menopausal oestrogen withdrawal (Nilas & Christiansen, 1987).

There are significant correlations of axial BMD with all three forearm sites. The strength of correlation between peripheral and axial BMD using DEXA is similar to some reported results for SPA and DPA (Madsen, 1976; Mazess et al, 1984). The study by Mazess et al (1984) used a distal one-third forearm region and the authors found a value of $r = 0.48$ for the lumbar spine BMD in 48 females aged 50–80 years. The study of Madsen (1976) on 41 females aged 20–93 years and five males aged 22–68 years gave a correlation coefficient of $r = 0.67$ using the same sites. A study of 63 British women comparing SPA at a distal one-third site and QCT of the lumbar spine gave a correlation coefficient of $r = 0.47$ (Compston et al, 1988). We found a greater correlation between ultradistal BMD and axial sites than with mid-distal or one-third radius. A similar pattern has been noted previously comparing DPA and SPA measurements (Schneider et al, 1988). Other studies have found similar correlation coefficients for different radial sites, but in these forearm BMD has not been measured at equivalent positions (Nilas & Christiansen, 1987).

The spread of axial BMD results for any one range of forearm BMD has in previous studies suggested that despite a significant correlation between these sites, forearm BMD cannot be used to predict axial BMD. Previous SEEs of axial from peripheral BMD using SPA and DPA have given values of around 0.12 g/cm^2 or 10–20% (Grubb et al, 1984; Nilas et al, 1985; Pocock et al, 1986; Wasnich et al, 1987; Schneider et al, 1988). We have found similar values with a range of 0.084–0.120 g/cm^2 (Table III).

Although it is not possible to predict accurately axial BMD from peripheral BMD, the forearm continues to be a useful, familiar and convenient site for BMD measurement. Forearm BMD can be used for the diagnosis of osteopenia and for following the effects of disease and therapy on bone mass, particularly in populations. It may also have a wider role in the prediction of future fracture, although until more prospective longitudinal data are available for spine and hip measurements, it is impossible to assess their relative values. The use of DEXA for forearm measurements has high precision and carries advantages of no requirement for a water bath, no radiation source and less radiation for the patient. For centres that already possess a suitable DEXA system the forearm can also be measured without acquiring extra equipment, and the scan time is the same as axial BMD. We have provided some initial data on normal British women to assist in the interpretation of results.

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Fat suppression in magnetic resonance imaging at low field strength using binomial pulse sequences

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Abstract. The use of binomial pulse sequences for fat suppression in MRI at low field strength (0.15 T) was investigated. Both spin–echo and inversion–recovery sequences were used and images obtained of the limbs, head and neck, and pelvis of volunteers and patients. Good fat suppression was seen particularly in small fields of view. Despite technical problems, chemical shift selective techniques can be applied at low field strength.

Chemical shift imaging is the general term used to describe magnetic resonance techniques that depend on differences in the resonant frequencies of different molecular species. Binomial pulse sequences (Hore, 1983) have been used to excite selectively either water or fat at a high field (1.5 T) where their resonances are separated by 3.3 ppm or about 200 Hz (Poon et al, 1989; Szumowski et al, 1989). Chemical shift images produced by this technique appear likely to be of considerable clinical value.

Much interest centres on whether or not similar results can be achieved at low magnetic fields where the separation between the resonant frequencies of water and fat is considerably less (*e.g.* 20 Hz at 0.15 T) making selective excitation of fat or water alone potentially more difficult.

In this paper we describe the implementation of binomial pulse sequences at a low field and illustrate their clinical use.

Methods and subjects

Imaging was performed on an 0.15 T Picker prototype machine. Two single-slice pulse sequences were developed. The first was a spin–echo (SE) sequence (time to repeat (TR) 1500 ms, time to echo (TE) 80 ms) (Fig. 1). The 90° pulse was a chemical shift selective binomial, 121, pulse centred on water. The interpulse spacing of the binomial pulse was chosen to be 25 ms to give 90° excitation of the water resonance and no net excitation at 20 Hz offset, *i.e.* the frequency of the lipid resonance. This composite pulse is followed by a slice-selective 180° pulse.

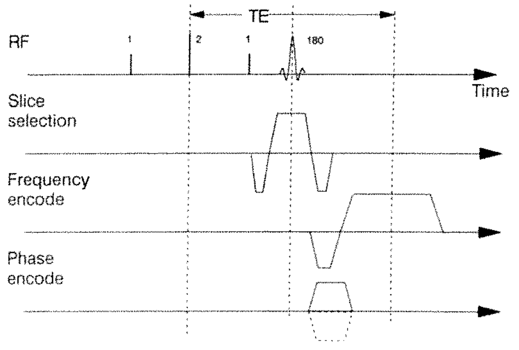

Figure 1. T_2-weighted SE sequence with binomial 90° pulse.

The second approach used an inversion–recovery (IR) sequence (Fig. 2) with an initial binomial (242) 180° pulse to cause inversion of fat but not water. Then, at a time to inversion (TI) adjusted so that fat had relaxed to the null point, a slice-selective 90° pulse was applied. This resulted in the excitation of water alone, which was

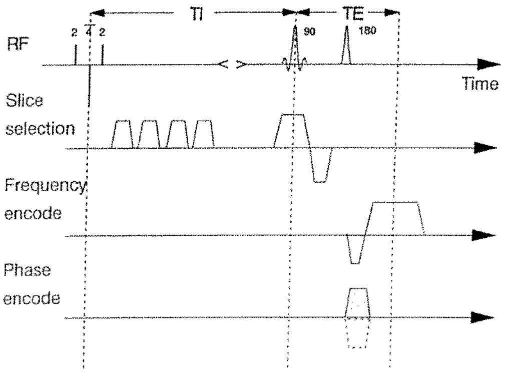

Figure 2. IR sequence with binomial 180° pulse.

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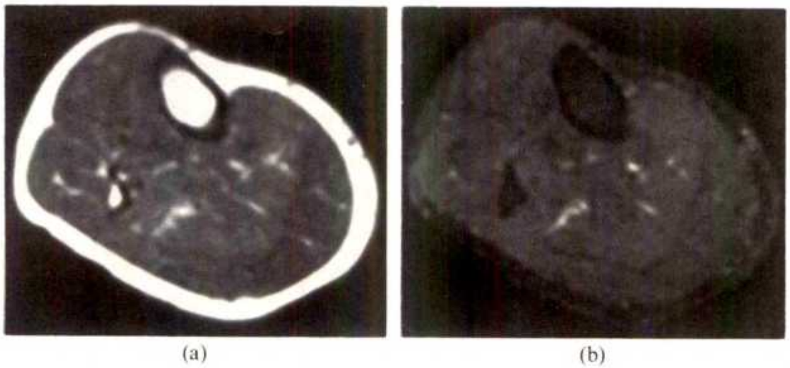

(a) (b)

Figure 3. Images of the leg of a volunteer. (a) Conventional T_2-weighted SE (1500/80). (b) Binomial pulse T_2-weighted SE (1500/80) showing suppression of signal from fat.

subsequently imaged. TR was varied down to 500 ms to give a T_1-weighted sequence. TI was varied from 60 ms to 120 ms. A TE of 44 ms was used. This is similar to a sequence described by Szumowski et al (1989) for use at high field strength. The advantage of these sequences over a conventional short TI inversion–recovery (STIR) sequence is that tissues with a short T_1, but with a chemical shift differing from that of fat, should not be suppressed by the binomial sequence.

The sequences were tested in volunteers and patients, with images of the limbs, head and neck and pelvis.

The field homogeneity is adjusted for each study. Shimming is performed on the Fourier transform of the free induction decay with the aim of maximizing the height of the water peak and the separation between the water and fat peaks. This additional shimming procedure can be readily performed in 3–5 min.

Results

Using the SE sequence, good suppression of both subcutaneous and bone marrow fat was seen in the limbs of volunteers (Fig. 3). Using the binomial IR sequence, optimal fat suppression was obtained with a TI of 80 ms compared with a TI of 100 ms for the non-chemical shift selective STIR at this field strength (Fig. 4). In patients with musculoskeletal tumours of the limbs and head and neck, the binomial sequence showed abnormal tissue clearly against the suppressed signal from fat. Figure 5 is a binomial T_2-weighted SE image of the femur in a 27-year-old man with osteosarcoma. The tumour in the bone marrow and surrounding soft tissue is sclerotic. More peripherally, high signal is due to infiltration or oedema and the extent of this is clearly shown on this fat-suppressed image.

Figures 6(a) and 6(b) are of a 34-year-old man with recurrent chondrosarcoma of the upper cervical spine invading the spinal canal and involving the spinous process and surrounding soft tissue. The extent of the high-signal abnormality is more clearly appreciated on the fat-suppressed T_2-weighted SE sequence than on the conventional sequence.

Good fat suppression throughout the image depended on field homogeneity, and across small fields of view good field homogeneity could be obtained with uniform fat suppression. However, in larger areas such as the pelvis, field inhomogeneity led to non-uniform fat suppression with banding seen particularly at the periphery of the image (Fig. 7(b)). Even in these circumstances useful information may be obtained from central regions of the image as shown in Fig. 7. These images are of a patient with known prostatic carcinoma. High signal is seen on the fat-suppressed image posterior to the prostate gland. The scans were obtained in the post-operative period when urinary tract infection was present and the histological nature of the change is unknown.

Discussion

Chemical shift selective sequences using selective saturation (Bottomley et al, 1984; Rosen et al, 1984) or

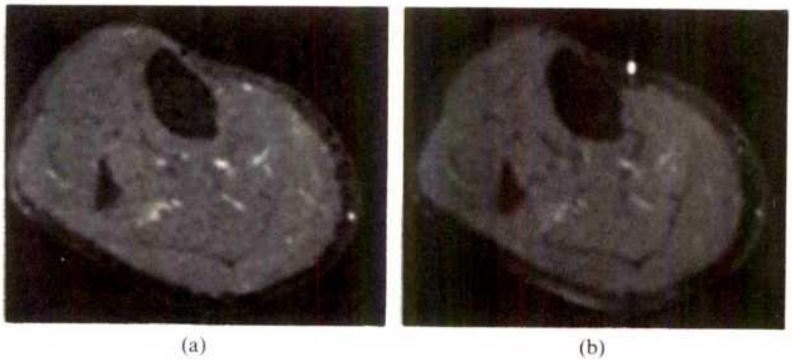

(a) (b)

Figure 4. (a) STIR (1500/44/100) of the leg of a volunteer. (b) Binomial IR (1500/44/80) showing similar fat suppression.

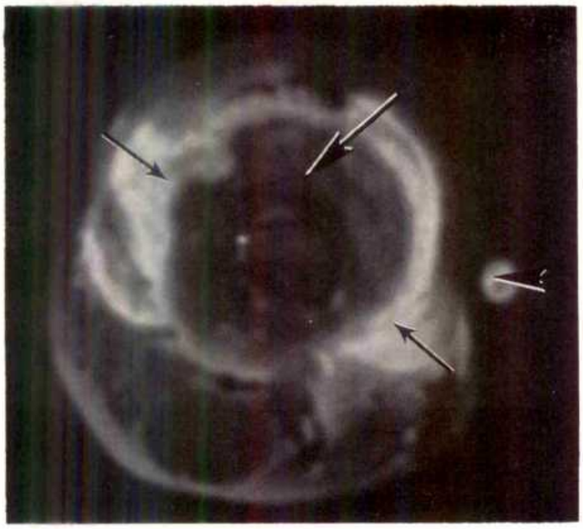
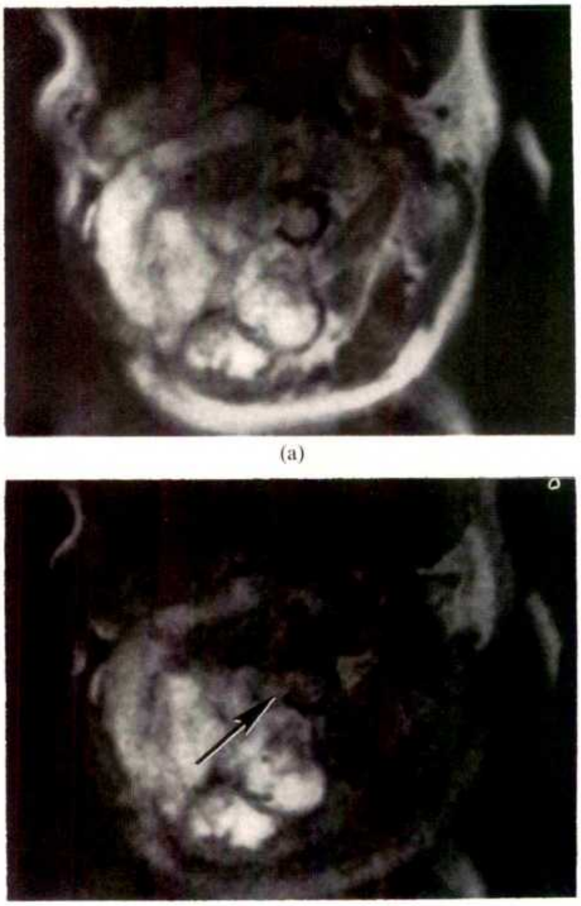


Figure 5. Binomial T_2-weighted SE (1500/80) of a patient with osteosarcoma of the femur showing sclerotic tumour (large arrow) and surrounding infiltration and/or oedema (small arrows). An external marker is present (arrowhead).

excitation (Haase et al, 1985; Joseph, 1985) have been used at high field strength and improved image contrast has been reported in the limbs Harned et al, 1990), abdomen and pelvis (Mitchell et al, 1989, 1991), including increased detection of lesions in patients with prostatic carcinoma (Rifkin et al, 1988). Another technique frequently used for fat suppression in clinical imaging studies is the STIR sequence (Bydder & Young, 1985). This sequence is easy to implement and is tolerant of poor fields. However, fat is suppressed because of its short T_1 and other tissues with similar short T_1 values will also be suppressed. This may include tissues enhanced by intravenous paramagnetic contrast agents. Frequency selective sequences cause suppression of the signal from fat due to its chemical shift and there have been reports of improved visualization of contrast enhancement (Simon & Szumowski, 1989), for instance in the orbit (Hendrix et al, 1990; Tien et al, 1991) and kidneys (Semelka et al, 1991), when these techniques have been used in combination with intravenous paramagnetic contrast agents.

The previous work on chemical shift selective saturation and excitation sequences has been performed at high field strength. These sequences are more difficult to implement at low field strength. The chemical shift between fat and water is about 3.3 parts per million. Although the chemical shift in parts per million is independent of field strength the difference in frequency varies with field strength. Thus at 0.15 T the frequency difference between fat and water is approximately 20 Hz compared with 200 Hz at 1.5 T. If the magnetic field varies across the field of view by a similar amount, *i.e* 3.3 ppm, there may be areas in the image in which water is suppressed rather than fat. Good magnetic field homogeneity is a function of magnet design and varies from one site to another. In principle, however, since T_2 for any tissue varies little over the range of fields used in MRI, the line widths of the fat and water resonances are wider in relation to the difference between them at low field than at high, which makes it more difficult to select a given resonance at a low field strength.



(a)

(b)

Figure 6. Transverse scans of the upper cervical spine of a patient with recurrent chondrosarcoma. (a) T_2-weighted SE (1500/80) and (b) binomial T_2-weighted SE (1500/80). Tumour is seen invading the spinal canal (arrow). The extent of the high signal abnormality in the spinous process and surrounding soft tissue is more clearly appreciated on the fat-suppressed image.

Another disadvantage of a low field for these techniques is that the interpulse spacing of the binomial pulse has to be longer in order to have the same chemical shift effect. We have used an interpulse spacing of 25 ms at 0.15 T whereas at 1.5 T spacing of 2.5 ms would be used. This longer spacing limits the minimum TE that can be obtained in the SE sequence and for this reason the IR sequence was applied.

We have shown that even at 0.15 T, with fat/water separation of 20 Hz, good fat suppression can be

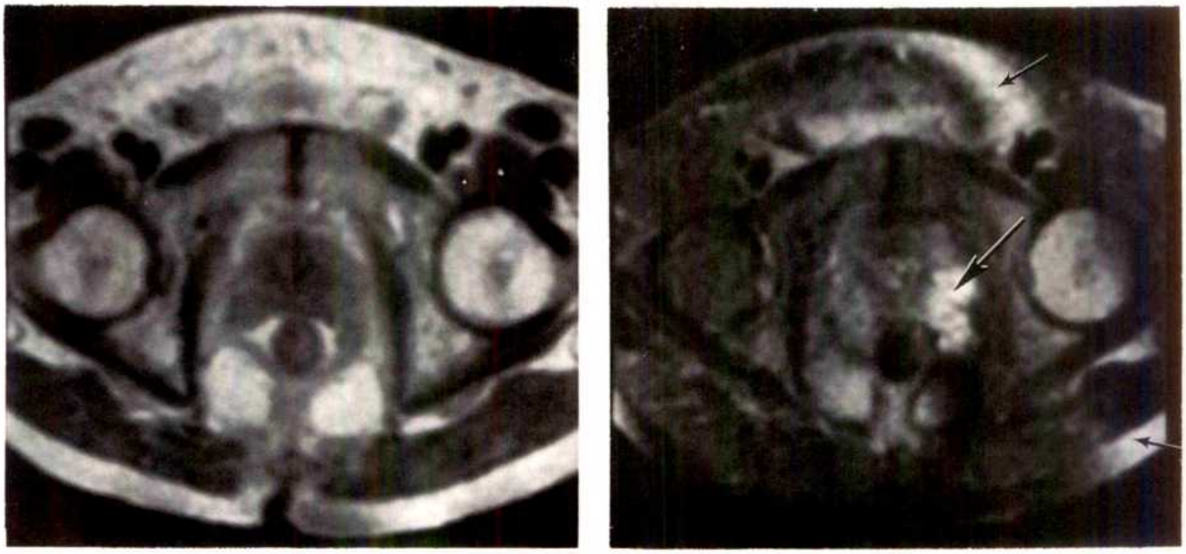

(a) (b)

Figure 7. Post-operative scan of a patient with prostatic carcinoma and urinary tract infection. (a) T_1-weighted SE (544/44) and (b) binomial T_2-weighted SE (1500/80). Peripheral high-signal banding due to artefact is shown (small arrows). High signal posterior to the prostate gland is shown on the left (large arrow).

obtained using binomial pulses for chemical shift selective excitation, particularly in small fields of view. Artefacts due to field inhomogeneity can be a problem in larger regions. A possible method of overcoming this problem is to shim on the specific small region of interest to ensure good field homogeneity in this area.

We found that optimal fat suppression occurred at a TI of 80 ms in the binomial IR sequence whereas in the conventional STIR sequence a TI of 100 ms is used. This difference is probably due to the conventional STIR sequence being optimized for adipose tissue, which contains approximately 15% water (International Commission on Radiological Protection (ICRP), 1975) whereas the binomial sequence suppresses signal only from the lipid itself.

In summary, despite the technical difficulties compared with high field we have demonstrated that chemical shift selective pulses for fat suppression can be implemented at low field strength.

Acknowledgment

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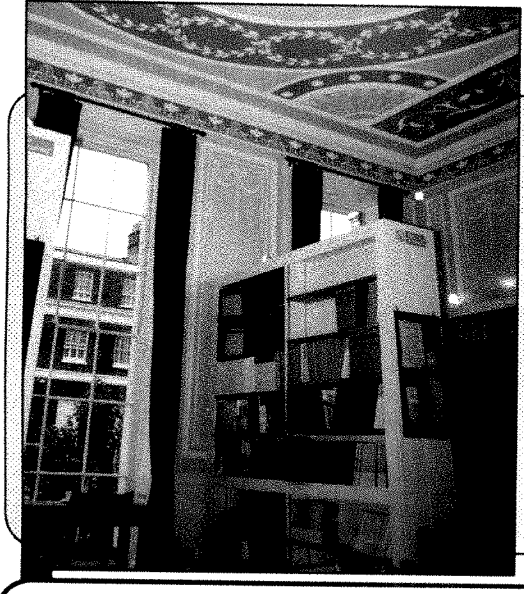

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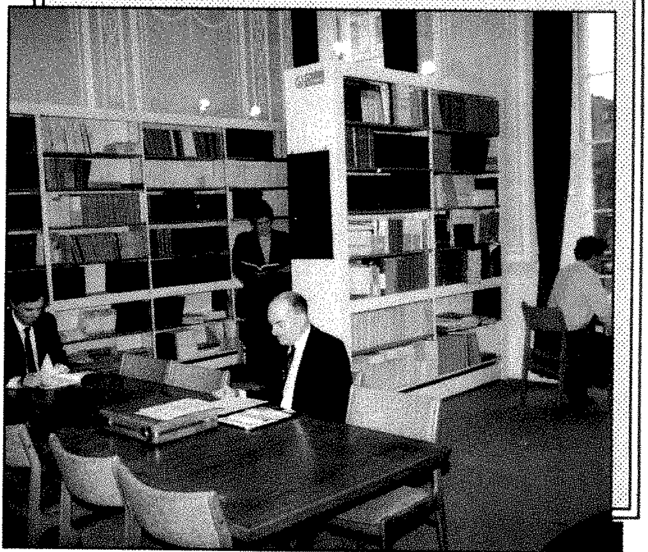

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Co-editors: A. Bakker, D. Bell, P. Kofakis, R. Mattheus, D. Meyer-Ebrecht, R. Van de Velde, T. Wendler

1992. Approx. 350 pp. 124 figs. 30 tabs. Hardcover DM 278,– ISBN 3-540-54592-1

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Duplex Doppler ultrasound in the investigation of occult nephropathy following haemolytic uraemic syndrome

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Keywords: Doppler, Nephropathy, Haemolytic uraemic syndrome

Abstract. Duplex doppler ultrasound has been reported to be of value in the detection of raised vascular resistance, particularly in the renal tract. A prospective single blind study investigating the use of duplex Doppler ultrasound to measure resistive index (RI) in patients with impaired renal function and a history of diarrhoea-associated haemolytic uraemic syndrome (D+ HUS) was performed. There was considerable overlap in the range of RIs, with RIs greater than 70% in children with normal renal function and in those with renal impairment following D+ HUS. There was no significant difference in the mean RI between the groups studied. We feel that the RI is not of value in predicting the presence of occult nephropathy following haemolytic uraemic syndrome.

The haemolytic uraemic syndromes (HUS) are a heterogeneous group of disorders characterized by haemolytic anaemia, thrombocytopenia and renal failure (Gasser et al, 1955). Two main subgroups are now recognized: the first is associated with a diarrhoeal prodrome, D+ HUS, and is a major cause of acute renal failure in Britain; the second is rare in childhood and has no antecedent diarrhoea, D−HUS (Levin & Barratt, 1984). Most children with D+ HUS make a full recovery, but 15% or more may develop some form of renal impairment (Milford & Taylor, 1990). Patriquin et al (1989) have recently proposed the use of resistive index (RI) to predict recovery from oliguria or anuria during the acute phase of D+ HUS. This observation led us to attempt to detect those children with chronic renal impairment following an episode of D+ HUS using duplex Doppler ultrasound.

Patients and methods

This was a prospective single blind study using Doppler ultrasound to assess renal and intrarenal blood flow in an attempt to recognize those children with impaired renal function following an episode of D+ HUS. Three groups of age and sex matched children were selected for study.

Group 1. Eight children with a history of D+HUS and a glomerular filtration rate of less than 80 ml/min/1.73 m^2 surface area (SA).

Group 2. Eight children with a history of D+ HUS and a glomerular filtration rate greater than 80 ml/min/1.73 m^2 SA.

Group 3. Normals. Nineteen children with normal renal function and no history of renal disease.

The ultrasound examinations were performed by two experienced sonographers, unaware of the medical history and renal function of the patient at the time of the examination. The renal and intrarenal arteries were examined with duplex Doppler ultrasound and a total of five measurements taken from each kidney. The RI was calculated from these measurements as peak systolic velocity minus end diastolic velocity divided by peak systolic velocity, which was calculated by the machine. A mean RI was calculated from the five readings. All examinations were performed with an Acuson 128 machine using real-time and pulsed Doppler scanning. The glomerular filtration rate (GFR) was estimated from the plasma clearance of chromium-51 edetic acid (Chantler & Barratt, 1972).

Results

Thirty-five children were studied: 19 children in the normal group, and eight in each of the groups previously affected by D+ HUS. The results are summarized in Fig. 1. There was a wide range of values measured in all three groups, with a range of 30.9% seen in the normal children, Group 3, and 31.1% seen in Group 1. There was considerable overlap in the RIs measured in all three groups. The lowest RI measured in all three groups was similar: Group 1, RI = 47.0%; Group 2, RI = 48.6%; and Group 3, RI = 45.0%. The highest RI, 78.1%, was measured in a child with a GFR of 37 ml/min/1.73 m^2 SA, but measurements of 75.9% and 75.4% were obtained in the group of normal children. The means of the three groups were similar: Group 1 mean 57.1%, Group 2 mean 56.9% and Group 3 mean 59.9% (Table I). The results were compared using paired Students' *t*-test, and showed no significant differences.

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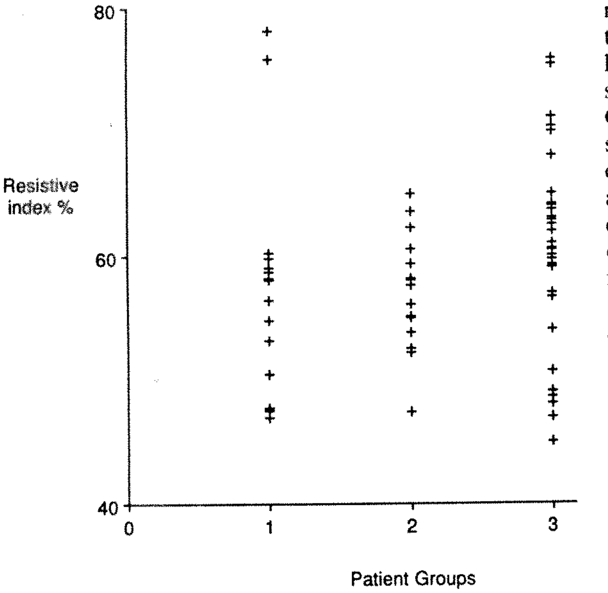

Figure 1. RIs measured in the three groups of children.

Discussion

Chronic renal impairment is the most serious long-term conseqence of D+ HUS. The development of a non-invasive and easily reproducible means of detecting children with renal impairment secondary to D+ HUS would be a significant advance in their care, avoiding radioisotope injection, day admission and two venepunctures in young children. The recent paper by Patriquin et al (1989) advocated the use of the RI in the acute phase, and demonstrated their ability to predict the time of recovery from the oliguric or anuric phase of the syndrome. The histopathological change seen in the acute phase is an alteration of the endothelium, with swelling of endothelial cells effectively narrowing the capillary lumen (Levin et al, 1989). The presence of arteriolar occlusion increases the intrarenal vascular resistance, increasing pulsatility leading to a high RI (Patriquin et al, 1989). As the kidney recovers, the intrarenal vascular resistance falls with a consequent fall in the RI (Patriquin et al, 1989). In those children with chronic renal impairment the histopathological changes are less specific. Tubular atrophy, interstitial fibrosis and glomerular segmental sclerosis may all occur. These changes should also raise intrarenal vascular resistance resulting in a high RI. It would be reasonable therefore to expect a higher RI to occur in the children with the lowest GFRs, Group 1. The highest RI recorded in our series, 78.1%, was found in the child with the lowest GFR, 37 ml/min/1.73 m^2 SA. However, his kidneys were sonographically abnormal, being small and of increased echogenicity. There were no other sonographically abnormal kidneys, and it may be that a significant elevation of RI only occurs in kidneys clearly abnormal on conventional real-time ultrasound in which measurement of RI would be of little benefit.

Table I. Ranges and means of the RIs in the three groups

Group	Range (%)	Mean RI (%)
1	47.0–78.1	57.1
2	48.6–65.0	56.9
3	45.0–75.9	59.9

The initial enthusiasm for the use of the RI in the assessment of renal and intrarenal blood flow has recently diminished with an increasing number of papers questioning its value (Genkins et al, 1989; Kelcz et al, 1990; Drake et al, 1990; Grant & Perrella, 1990). The normal range of RI and its alteration with age have not been established, and the wide range of values seen in our group of normal children questions the previous use of absolute measurements to predict disease. A significant change occurs with alteration of heart rate (Mostbeck et al, 1990), and it is known that other factors such as compression of the kidney by the ultrasound probe may cause an elevated RI (Pozniak et al, 1988). We suggest that RI is not as useful as was initially reported, and raise doubts about the use of RI in detecting chronic renal impairment.

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Percutaneous transluminal angioplasty: pain during balloon inflation

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Abstract. The pain during the balloon dilatation of angioplasty was evaluated prospectively to assess its clinical significance. In 54 angioplasties, no pain was observed in 54%, mild pain in 20%, moderate pain in 11% and severe pain in 15%. Moderate or severe pain was observed in 39% of 28 iliac angioplasties and in 7% of 14 femoral angioplasties. There was a significant difference between the two groups. We did not find any significant correlation between the severity of pain and stenotic ratio before angioplasty. Severe pain may be a warning of severe dissection; in our study, all severe dissections were accompanied by severe pain without arterial rupture.

Patients often experience some degree of pain during inflation of balloons for angioplasty, not associated with clinical problems. However, some authors have suggested that severe pain may be an important warning of arterial rupture (Jensen et al, 1985; Chong et al, 1990). The frequency and severity of pain during balloon inflation has not been reported. We have evaluated prospectively the pain experienced by patients to determine its clinical significance.

Materials and methods

The study comprises 54 angioplasties in 44 patients with atherosclerosis: 28 iliac, 14 femoral and 12 renal arterial dilatations. Technical failures such as subintimal passage of the guidewire or catheter were excluded in this study. Angioplasties were performed in a routine fashion under local anaesthesia (Korogi et al, 1987). The balloon required was selected by measuring the diameter of the contralateral artery or the adjacent patent portion of the vessel on the conventional angiogram. The diameters of the balloons used were 6–8 mm in iliac angioplasty and 4–6 mm in femoral or renal angioplasty. An oversized balloon was never used. The balloon was inflated by hand twice for 30 s, or several times until the "waist" of the balloon disappeared under fluoroscopy. We did not use a pressure gauge because of loss of feeling at inflation and dilatation of the stenosis. However, the syringe size used was larger than 10 ml capacity to avoid excessive pressure.

Patients were asked to report any pain they experienced, and angiographers recorded the patient's distress and motion during balloon inflations. The data were scored from zero to 3 by the following criteria: (0) no pain; (1) mild pain (no distress or motion); (2) moderate pain (face being distorted or moving slightly); and (3) severe pain (giving a cry or major movement).

The site of dilatation, the stenotic ratio before dilatation and the luminal diameter after dilatation were correlated with severity of the pain. Severe dissection after dilatation was defined as an intimal dissection compromising flow and requiring further therapy, although intimal dissection itself was a common finding at the dilatation site. The unpaired *t*-test was used in the statistical evaluations.

Results

In 54 angioplasties, no pain was observed in 29 dilatations (54%), mild pain in 11 (20%), moderate pain in six (11%), and severe pain in eight (15%) dilatations. The pain was observed only during balloon inflation. In a few patients, however, pain continued for several to 10 s after deflation of the balloon.

No dilated artery ruptured in this study. However, severe dissection occurred in three dilatations (two iliac and one femoral), and was associated with severe pain. In these two patients with iliac angioplasty, no other symptoms related to severe dissection were present. They were referred for bypass surgery because of unsuccessful re-dilatation, which also produced severe pain. Another patient with femoral angioplasty complained of temporary pain in the lower leg after occurrence of severe dissection, and immediate re-dilatation, which did not produce severe pain, was performed successfully. Data of the re-dilatations are not included in this evaluation. No overdistension was observed in our series.

Analysis of the data regarding the site of dilatation demonstrated a significant difference between iliac and femoral angioplasties ($p < 0.05$) (Table I). Eleven of 28 iliac angioplasties (39%) had moderate or severe pain against only one of 14 femoral angioplasties (7%). There was still a significant difference between the two when the three cases of severe dissection were excluded from analysis ($p < 0.05$). Although the mean score was

Table I. Mean score of pain with regard to site of dilatation

Site of dilation	Total	Severity of pain (no. of patients)				Mean score
		None	Mild	Moderate	Severe	
Iliac	28	10	7	5	6[a]	1.25
Femoral	14	10	3	0	1[b]	0.43
Renal	12	9	1	1	1	0.50
Total	54	29	11	6	8	0.87

[a] Two cases of severe dissection.
[b] One case of severe dissection.

Table II. Mean score of pain with regard to stenotic ratio

Stenotic ratio (%)	Total	Severity of pain (no. of patients)				Mean score
		None	Mild	Moderate	Severe	
50–60	19	10	5	3	1	0.74
61–75	10	4	3	1	2	1.10
76–90	10	7	1	0	2[a]	0.70
91–100	15	8	2	2	3[b]	1.00
Total	54	29	11	6	8	0.87

[a] Two cases of severe dissection.
[b] One case of severe dissection.

also low in renal angioplasty, there was no statistical significance between iliac and renal arterial dilatations because of small numbers.

We did not find any significant correlation between the severity of pain and stenotic ratio before angioplasty (Table II). Severe stenosis did not necessarily cause severe pain.

Discussion

Not only vasomotor nerves but also sensory nerves are present in the walls of blood vessels. However, these nerves are not found in the intima or media, but are present in the adventitia on electron microscopy (Bloom & Fawcettt, 1975). The sensory nerves are myelinated, and register a sensation of pain caused by a penetrating object or a sudden distension of the vessel (Rhodin, 1974). It has been suggested that pain during balloon inflation represents adventitial stretching (Katzen, 1983). Our previous study showed a varying degree of adventitial stretching as well as intimal dissection and medial overdistension after experimental angioplasty in rabbits (Korogi & Takahashi, 1987).

In the large elastic arteries, such as the aorta, subclavian and common iliac arteries, there are more sensory nerves than in the more peripheral muscular arteries (Rhodin, 1974; Bloom & Fawcett, 1975). The significant difference between the iliac and femoral arteries may be explained by a different distribution of sensory nerves.

Some authors have described severe pain as an important warning of arterial rupture, although this is an extremely rare complication. Patients often experience some degree of pain in many balloon angioplastic procedures (Jensen et al, 1985; Chong et al, 1990). Most interventional radiologists recognize that the pain during balloon inflation is usually of no clinical consequence. However, there has been no report about the exact frequency and severity of pain and its clinical significance in balloon angioplasty. Our evaluation revealed that the frequency of moderate or severe pain was up to 40% in iliac angioplasty, which might be much higher than previously expected. Severe pain may not be a warning of arterial rupture but of severe dissection; in our study all severe dissections were accompanied by severe pain without arterial rupture. In the iliac region, two of six cases (33%) with severe pain showed severe dissection, as did the one case in the femoral region (100%). Severe intimal dissection, not accompanied with clinical consequence, is presumed to occur much more frequently than arterial rupture.

In conclusion, moderate or severe pain occurred in up to 40% of iliac angioplasties. There was a significant difference in incidence of pain during the balloon dilatation of iliac and femoral angioplasties, which may be explained by the different distribution of sensory nerves. Furthermore, severe pain may be a warning of severe intimal dissection.

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Mitomycin C, 5-fluorouracil and radiation in advanced, locally recurrent rectal cancer

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Abstract. 15 patients with inoperable presacral recurrent rectal cancer following surgery were treated with combined radiation and chemotherapy. Treatment consisted of split-course radiotherapy with 50 Gy in 25 fractions over 5 weeks and, after 4 weeks, an additional 20 Gy in 10 fractions over 2 weeks. At the start of treatment and following the split course, chemotherapy was administered. Mitomycin C was given on Day 1 (dose: 15 mg/m^2 i.v. bolus) and 5-fluorouracil from Day 1 to Day 5 (dose: 750 mg/m^2/24 h, continuous i.v. infusion). Owing to considerable, predominantly haematological and gastrointestinal toxicity, only six out of 15 patients received treatment according to the protocol. The symptomatic relief of symptoms was good. Pain was controlled in seven of eight symptomatic patients. Seven of the patients showed response according to computed tomography, but in none of these cases was a complete remission seen. After a follow-up of at least 30 months, only three patients are alive. The 1-, 2- and 3-year survival rates are 9/15, 6/15 and 3/12, respectively. The median survival is 14 months (range 4-60+ months). In comparison with historical data from the same institution, combined radio-chemotherapy did not show any prolongation of survival or increased response rate, but increased toxicity excessively, when compared with radiation alone.

Following apparently curative surgery for rectal cancer, locally recurrent tumours are seen in 30% (unselected patients) to 70–80% (high-risk patients) of cases, depending on stage of disease, site of primary tumour and histopathological grading (Olsen et al, 1980; Rao et al, 1981; Påhlman & Glimelius, 1984; Athlin et al, 1988). Even though highly specialized centres have reported considerably lower rates (Morson & Bussey, 1967; Heald & Ryall, 1986), local recurrences substantially contribute to morbidity and mortality in this group of cancer patients. A large number of patients will eventually succumb to their locally recurrent tumour without evidence of distant metastases (Cass et al, 1976; Chung et al, 1983; Pheils et al, 1983).

Only very few patients, predominantly with small recurrences following anterior resection, are amenable to undergo surgery for potential cure. Radiotherapy is considered standard treatment for locally recurrent rectal cancer. Though radiotherapy offers good palliation in most cases, cure is rarely achieved (Ciatto & Pacini, 1982; Dobrowsky, 1988; Herzog et al, 1988).

In an attempt to improve results, a more agressive treatment protocol, combining chemotherapy with mitomycin C (MMC), 5-fluorouracil (5-FU) and radiation was initiated. Both 5-FU and MMC have been used alone and together with radiation in treatment of gastrointestinal tumours, especially in anal canal cancers where this combined-modality treatment is now considered standard therapy by many radiation and surgical oncologists.

The present pilot study was initiated in 1985 following encouraging results in squamous cell cancers of the anus and upper aerodigestive tract with a regimen consisting of radiotherapy and concomitant administration of MMC and 5-FU.

Materials and methods

Patients

Between September 1985 and April 1988, 19 patients with advanced locally recurrent rectal cancer were entered in the study. For various reasons (stated later) four patients were excluded from this analysis. In all 15 evaluable patients, the site of the recurrent tumour was the presacral region, and all patients had been considered inoperable by the referring surgeon. There were nine male and six female patients aged 43 to 72 years (median 60 years).

All patients initially had undergone intended curative resection of their tumour 1–43 months (median 10 months) prior to development of their relapse. 10 patients initially had an abdomino-perineal resection, and five patients an anterior resection. Seven patients were classified as Dukes B and eight as Dukes C stage of disease initially. All histologies were adenocarcinoma: well (2), moderately well (6), poorly differentiated (3); in four cases no differentiation was specified.

Most patients (12/15) had symptomatic disease, with pain present in eight, discharge and bleeding in three, hydronephrosis in three and neurological symptoms in four. In 10 out of 15 patients the level of carcinoembryonic antigen (CEA) was elevated (see Table I).

One patient had undergone resection of liver metastases, and was considered free of macroscopic distant disease; all other patients were initially free from detect-

Table I. Symptoms and signs of disease and their response to therapy ($n = 15$)

Symptom	No. of patients	Response
Pain	8	7
Hydronephrosis	3	2
Discharge/bleeding	3	2
Neurological symptoms	4	2
Elevated CEA	10	8
Computed tomography	15	7*

*Only 14 out of 15 underwent post-therapeutic CT scanning.

able distant metastases following surgery and at the start of radiation therapy. All patients had a Karnofsky performance status of 50% or more at presentation.

Reasons for exclusion

Four patients were excluded from this analysis. One patient had widespread liver metastases and three patients discontinued treatment at an early stage. None of these patients had any treatment-related side-effects that might have been the reason for not completing the therapy.

Treatment

The treatment consisted of a combination of radiation and systemic chemotherapy using MMC and 5-FU administered simultaneously with radiation. MMC was given before the first radiation, on Day 1, the dose being 15 mg/m^2, administered by intravenous bolus injection. From Days 1 to 5, the patients received a continuous infusional administration of 5-FU at a rate of 750 mg/m^2/24 h. During the first course of radiation a dose of 50 Gy/25 fractions over 5 weeks was given. Following a split of 4 weeks another course of chemotherapy, as above, and an additional dose of 20 Gy/10 fractions/2 weeks was planned.

The volume irradiated consisted of the actual recurrent tumour, as outlined in computed tomographic (CT) scans, with a 3–4 cm margin. Usually a four-field box technique or a rotation technique was used. All patients received their radiation treatments by megavoltage equipment (Siemens 42 MeV Betatron or 6 MeV Mevatron) or telecobalt (Siemens Gammatron).

Assessment

All patients were followed regularly and none were lost to follow-up. Prior to therapy, all patients had blood tests for evaluation of renal and liver function, a complete blood count and evaluation of the carcinoembryonic antigen (CEA). One month following therapy, an assessment regarding objective and subjective tumour response was performed. The minimum follow-up in this series was 30 months, with 12 out of 15 patients having had treatment 3 years before assessment. Survival was determined from the start of radiotherapy and assessment by November 1990.

Results

Treatment tolerance

Owing to side-effects, the full dose of radiation (50+20 Gy) with two courses of chemotherapy could not be given to all patients. Only six of the 15 patients received treatment as planned; five patients received the full radiotherapeutic dose, but only one course of chemotherapy, while four patients were treated with 50 Gy and one course of MMC and 5-FU. The reasons for omitting the second course of chemotherapy and/or full dose of radiation were significant haematological side-effects and lack of tumour response.

The side-effects mainly consisted of neutropenia and thrombopenia, which were present in five out of 15 patients. The side-effects are listed in detail in Table II. Late side-effects have consisted of decreased bladder capacity owing to moderate cystitic reaction. No major late side-effects have been recorded from the small bowel. The number of patients at risk, however, is very low because of overall short survival.

Response to therapy

Two-thirds (10/15) of patients responded to therapy, response being defined as any decrease of symptoms or improved radiological findings following therapy. Of the eight patients who had severe pain initially, seven responded well to therapy, and two out of three patients with hydronephrosis benefited. Of the 14 patients on whom repeat CT scans were performed, only seven showed any kind of response, while in seven cases there was no change compared with initial CT scans. In none of the patients who responded could a complete remission be recorded.

Only one of four patients who received the lower dose (50 Gy) showed any response; of the other 11 patients, nine responded to therapy. The median duration of pain relief was 6 months.

Survival

The overall outcome was poor. The median survival was 14 months, ranging from 4 to 60+ months. After a minimum follow-up period of 30 months, only three out of 15 patients are alive, of whom one has incurable

Table II. Side-effects of combined radio–chemotherapy in recurrent rectal cancer ($n = 15$)

Symptom	No. of patients
Haematological	5[a]
Nausea/vomiting	5[b]
Diarrhoea	3[c]
Cystitis	3
Orchitis	2
Moist skin desquamation	4

[a] WHO Grade 1 in two patients, Grade 3 in two patients and Grade 4 in one patient.

[b] WHO Grades 1–2.

[c] WHO Grades 2–3.

disease. One patient who died at 14 months showed no disease at autopsy. The other 11 patients died with uncontrolled local disease. Four of the deceased patients had also developed distant metastases: two with lung, one with brain and one with liver metastases. The survival rate at 1 year was 9/15 and at 2 years 6/15. The 3-year survival rate was 3/12.

Discussion

One of the major problems that develops in rectal cancer is due to the fact that local recurrences develop. Locally recurrent rectal cancer is generally a fatal disease for most patients, and only very few cases with small relapses at the site of the anastomosis following low anterior resection can be saved by surgery. Most patients who die from rectal cancer do this with local relapse as part of their disease in as many as 75% of cases (Taylor, 1962).

Although long-term survival is infrequent, radiotherapy often is able to decrease symptoms, especially pain, in these very unfortunate patients and thus is able to increase quality of life for at least a short time. In the present study, pain relief was achieved in seven out of eight patients. This number is in accordance with the literature, quoting 60–90% of patients who experience pain relief (Bohndorf et al, 1984; Schmidt et al, 1984; Dobrowsky & Schmid, 1985; Herzog et al, 1988). In a previous analysis of patients treated with radiation for presacral recurrences, the effect of radiation on pain was independent of dose (Dobrowsky & Schmid, 1985). The present study does not allow any conclusion on this; only one patient, receiving the lower dose (50 Gy), did not experience any pain relief.

Overgaard et al (1984) were able to record a complete response in 40% of patients irradiated with more than 56 Gy. In the present series only 50% of patients showed any decrease in size of their recurrence as measured by CT scans and in none of the cases was a complete response achieved. This seems to be the rule, as most authors do not see any notable decrease in tumour size, even at higher doses, above 60 Gy (Bohndorf et al, 1984; Flentje et al, 1988).

Through past experience of very poor results and prognoses using radiotherapy in recurrent rectal cancer, the decision was made to add chemotherapy to the treatment. The choice of using MMC and 5-FU was based on the fact that both these drugs have been used for treatment of gastrointestinal tumours with reported response rates of 18–45% (Buroker et al, 1978; Krauss et al, 1979; Tseng et al, 1981). The mode of administration of 5-FU chosen was by infusion. Seifert et al (1975) noted significantly less side-effects when 5-FU was infused compared with when it was given as a bolus injection.

Clinically, MMC and 5-FU were initially used together with radiation in anal cancers treated pre-operatively (Nigro et al, 1974). The Detroit group also used the same drug combination for pre-operative radiation treatment of rectal cancers, but saw a high incidence of haematological toxicity, which necessitated a dose reduction (Buroker et al, 1976). The initial dose of MMC was 20 mg/m^2, injected as an i.v. bolus once, and the dose of 5-FU was 1000 mg/m^2/24 h for 5 days. Later, the group lowered the doses of both MMC and 5-FU because of inacceptable toxicity.

Experimental findings have suggested that 5-FU and radiation interact in either an additive way (Weinberg & Rauth, 1987) or supra-additively (Byfield et al, 1982) and that the drug level should be maintained for a longer period of time (at least 24–48 h) following radiation. *In vitro* and *in vivo* experiments examining the mode of interaction of MMC and radiation tend to favour the additive interaction theory (Rauth et al, 1983; Rockwell, 1983). MMC has been used with 5-FU, without radiation, and was considered to have a greater than additive interaction in an *in vivo* experimental model using Sarcoma 180 ascites cells that had been injected intraperitoneally in mice, when survival was the experimental end-point (Sartorelli & Booth, 1965).

Whether the addition of chemotherapy is of benefit to the patient is questionable. In the present, small study, MMC and 5-FU definitely added to the toxicity, but there was no clear benefit regarding survival or symptomatic pain relief, when compared with previous data (Dobrowsky & Schmid, 1985). Regarding survival of patients the 1-, 2- and 3-year survival rates were 60%, 40% and 25% in the present radio–chemotherapy protocol versus 69%, 29% and 12%, respectively, in the historical series (Dobrowsky & Schmid, 1985). Generally, 3-year survival rates of 0–12% are reported (Rousseau et al, 1969; Vongtama et al, 1975; Ciatto & Pacini, 1982). Owing to the small series presented in this report, there is no certain difference compared with previous reports from the same institution (Dobrowsky & Schmid, 1985; Dobrowsky, 1988). Comparing the median survival, the combined treatment has not shown any advantage: 14 months versus 20 months in the historical control. Only by a randomized trial would it be possible to determine any benefit of this combined-modality therapy versus radiation alone.

The use of chemotherapy and radiation has lead to an enhanced effect. This enhancement has not resulted in any increase in tumour response, but has considerably increased the side-effects. Similar results have been obtained by others. Danjoux and Catton (1979) noted only minor acute reactions, but saw 29% late complications when 5-FU was administered concomitant with split-course radiation. In a later trial examining split-course and continuous radiation with 5-FU, 69% of patients experienced severe acute reactions when treated with continuous radiation compared with only 21% in the split-course regime (Danjoux et al, 1985). The high complication rate is partly due to the continuous radiation and partly due to the portal arrangement, using parallel opposed fields to treat large volumes. Sischy (1985) reported a good response when using a similar regime for large inoperable primary rectal cancers. This reflects the large biological difference between a fairly well vascularized primary tumour and an inoperable, large recurrent rectal cancer, which is normally not well vascularized and, thus, contains a large number of hypoxic radioresistant cells.

Some authors have reported a better effect when MMC and 5-FU were administered intra-arterially (Patt et al, 1985; Piroth et al, 1986) compared with systemic i.v. administration. Improvements might be possible when the drugs are administered intra-arterially with simultaneous radiation. First experiences with this approach have yielded very good responses, but no long-term benefit has been recorded (Dobrowsky, 1988).

In conclusion, this trial does not seem to show any apparent benefit for the combination of 5-FU and MMC administered systemically with simultaneous radiation in recurrent rectal cancer. Addition of chemotherapy to radiotherapy has not increased response or survival, but has increased toxicity unacceptably and cannot be recommended for routine use. No advantage of combined treatment was seen compared with radiation alone, which still must be considered palliative treatment of choice in these patients.

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Reduction in the diameter of human hairs following irradiation

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Abstract. A measurable reduction in hair diameter was observed in human hairs following single exposures to γ-rays, 250 KeV X-rays, 8 MV photons and 10 MV electrons in the range 2.9–14.0 Gy. The data from the different types of radiation were pooled and fitted by linear regression with a slope of $2.34 \pm 0.42\%$ Gy^{-1}. There was approximately 2.4% reduction in hair diameter per Gy exposure. It would appear that the measurement of damage to the matrix cells of growing human hairs exhibits potential for use in biological dosemetry, especially in cases of non-uniform overexposure.

Animal studies have shown that the matrix cells of actively growing hairs are a sensitive target of radiation damage with potential for development as a biological dosemeter.

Accidental exposures to radiation are frequently highly localized and non-uniform. The biological methods available to measure radiation overexposure that rely on the analysis of induced chromosome aberrations in lymphocytes are not usually capable of yielding regional information. Hairs have been proposed as a potential dosemeter because they are located over much of the body surface. They are rapidly proliferating and damage will be expressed in a short time-scale (Wells & Charles, 1982). Although epilation is a recognized phenomenon as a result of radiotherapy and chemotherapy, there are little data available on the dose required to produce hair loss.

Studies have been carried out using rodents and pigs as animal models. Radiation-induced changes in the distribution of pigment in matrix cells have been observed in rodents (Chen et al, 1981; Potten & Forbes, 1972; Vegesna et al, 1987, 1988). Potten et al (1990) and Geng and Potten (1990) observed a dose-dependent increase in the number of apoptotic fragments (nuclear fragments indicating cell damage or death) which correlated with a reduction in hair diameter. Damage to the matrix cells of actively growing pig and mouse hairs has been shown to result in a transient dose-related reduction in diameter (Potten, 1985, 1986; Sieber & Wells, 1986; Sieber et al, 1986).

This paper reports the results of a pilot study on the effect of radiation on the diameter of actively growing human hairs.

Methods

Ethical consent for this study was obtained from the Central Oxford Research Ethics Committee. Patients receiving either a single exposure of radiation or fractionated therapy to the chest, head or leg with an interfraction interval > 4 days were identified. Patients fulfilling these criteria, who had hairs in the treatment area, were approached and their informed consent was obtained.

Hair growth is asynchronous in man and pig, which makes the pig a good animal model (Meyer et al, 1978). In order to assess damage to the matrix cells of hairs in an asynchronous population, it was necessary to identify actively growing hairs, as dormant hairs were unlikely to express damage. To identify actively growing hairs, the hairs were shaved at the time of irradiation and it was assumed that any visible hairs after treatment had resulted from new growth.

The irradiation field and, when available, a nearby area outside the treatment area were shaved prior to irradiation; the latter provided a control field. Dosemetry was by thermoluminescent discs (TLD); three with 1 mm and three with 5 mm tissue-equivalent build-up were placed at the centre of the irradiation field at the time of treatment. Since the hair follicle lies at varying depths within the build-up region of the depth–dose curve from ^{60}Co γ-rays and 8 MV photons the dose to the hair follicle was taken as being the average of the measured doses at 1 mm and 5 mm depth. Calibration was by comparison with TLDs irradiated to known doses in a ^{60}Co beam using the relative sensitivity of individual groups of discs. The discs were read in a Harshaw 2000 D reader.

Radiation was given as prescribed using ^{60}Co γ-rays produced by a Mobaltron MS90, 250 kV X rays produced by a Philips RT250 or 8 MV photons produced by a linear accelerator. One patient was treated with a single 10 MeV electron beam (MEL SL75/10) to the head.

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Hair growth was assessed visually in patients either when they returned for their second treatment or, for patients receiving single doses, 5–7 days after irradiation. Hairs were collected by plucking with tweezers. The hairs were fixed to a microscope slide with double-sided adhesive tape and a magnified image (× 10) was projected onto a digitizer pad (Calcomp Ltd). Owing to the considerable variation in diameter both within an individual hair (Das-Chaudhuri & Chopra, 1984) and between different hairs, each hair was used as its own control. The diameter of the hair was measured at the cut end, *i.e.* the point at which it emerged from the skin surface at the time of irradiation. This was used as a "control" diameter, which was compared with the minimum diameter approximately midway between the hair bulb and the cut end. The point of narrowing on the hair to be measured was selected by eye. Human hairs are approximately cylindrical but there is an uneven deposition of keratin in curly hairs. Very curly hairs were excluded from the study. All hairs available from each irradiated field were measured, the number of hairs ranged from seven to 120 hairs.

Results

The percentage reduction in hair diameter was calculated for each hair and the mean ± SE was calculated for each field. The number of hairs sampled, mean (±SE) percentage reduction in hair diameter, body site, radiation type and dose delivered are given in Table I for each patient in the trial.

For unexposed control hairs the percentage reduction in hair diameter over the dose range 2–14 Gy for 8 MV photons, 250 kV X rays, electrons and ^{60}Co γ-rays is shown in Fig. 1. Where possible, control hairs were collected from an adjacent non-irradiated site. Where patients received treatment to the chest a large area was exposed to radiation and few hairs were found outside the irradiated area. Negative values for unirradiated hairs from the wrist, scalp, chest and leg were obtained because there was a gradual reduction in diameter after the hair emerged from the skin surface as the hair tapered to a point. This made the midpoint between the bulb and the cut end thicker than at the cut surface.

A line in Fig. 1 shows the percentage reduction in diameter of pig hairs following 250 kV irradiation (Sieber et al, 1986) and mouse guard hairs following ^{137}Cs γ irradiation (Potten, 1985). The data points from human hairs are displaced to the right of the line representing pig and mouse hairs, which suggests that the response of human matrix cells to irradiation was less than that of either pig or mouse. A regression line has been fitted to the percentage reduction in diameter for human hairs from 0 to 14 Gy, regardless of radiation quality (Fig. 1). A slope of 2.34 ± 0.42% Gy^{-1} was

Table I. The percentage reduction in diameter in human hairs following a single exposure to radiation

Body site	Radiation type	Dose (Gy) ± SD	Number of hairs measured	Mean percentage reduction in diameter ± SE
Chest	Control	0.0	14	−3.83 ± 2.38
	^{60}Co γ rays	13.6 ± 0.1	5	32.85 ± 6.32
		9.1 ± 1.0	70	10.97 ± 1.85
		5.5 ± 0.7	10	5.19 ± 1.25
		10.2 ± 1.1	39	12.71 ± 2.18
		6.1 ± 0.8	86	7.49 ± 1.62
		9.4 ± 1.2	20	25.16 ± 4.62
		9.8 ± 0.2	31	35.01 ± 2.71
	8 MV photons	7.4 ± 2.9	31	10.88 ± 3.36
		6.7 ± 2.0	32	15.39 ± 1.26
		7.4 ± 2.2	14	17.03 ± 2.84
	250 keV X rays	7.9 ± 0.5	14	12.04 ± 3.23
Leg	Control	0.0	15	1.92 ± 2.95
	8 MV photons	2.9 ± 1.2	41	10.44 ± 2.88
Scalp	Control	0.0	88	−6.76 ± 1.52
	10 MeV electrons	8.0 ± 0.2	117	8.57 ± 1.08
	250 keV X rays	3.9 ± 0.4	9	13.72 ± 5.36
		7.8 ± 0.1	25	21.05 ± 1.69

The number of hairs measured from each field exposed to radiation is shown along with the standard error of the mean (±SE) percentage reduction in hair diameter. Control measurements were taken, where possible, from an adjacent non-exposed area. The value given for the percentage reduction in diameter of hairs collected from the chest was the mean value obtained from several fields. The dose was calculated to allow for variation in the depth of follicles and was the mean of values obtained with and without build-up ± associated standard deviation (SD).

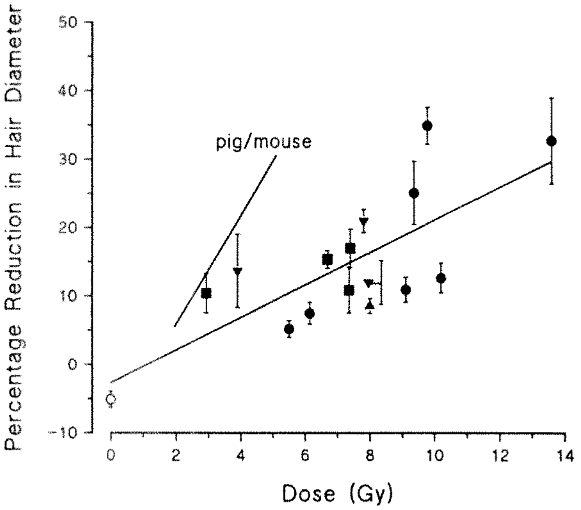

Figure 1. Shows the percentage reduction in diameter of human hairs following single exposures to ● ^{60}Co γ-rays, ■ 8 MV photons, ▼ 250 KeV X-rays, and ▲ 10 MV electrons and ○ unirradiated control. The percentage reduction in diameter in hairs from the pig following 250 KeV X-irradiation (Sieber et al, 1986) and the mouse following ^{137}Cs γ-irradiation (Potten, 1985, 1986) is shown displaced to the left of the linear regression line fitted through the human data. The error bars indicate ±SE.

obtained. This slope was significantly different from zero ($p < 0.001$). However, the value of $-2.28 \pm 3.12\%$ obtained for the intercept of the regression line was not significantly different from zero ($p = 0.4$).

The slope obtained for percentage reduction in diameter for pig hairs was $6.49 \pm 0.46\%$ Gy^{-1} (Sieber et al, 1986), *i.e.* significantly different from the human data.

Discussion

In rodents, hair matrix cells were found to be a radiosensitive target with a measurable reduction in DNA synthesis 30 min after irradiation (Malkinson & Griem, 1968). Changes in the number of matrix cells and distribution of pigment within these cells have been studied. Chen et al (1981), Potten and Forbes (1972) and Vegesna et al (1987) found an alteration in the distribution of pigment in mouse hairs following irradiation. Potten et al (1990) also found changes in the number of medullary cells and in micronuclei formation following doses of ^{137}Cs γ-rays over the range 0.2–6.0 Gy. At higher doses, damage to the matrix cells resulted in large numbers of apoptotic fragments and damage could not be assessed. Geng and Potten (1990) related the number of apoptotic fragments to the reduction in hair diameter and found both to be dose dependent over the range 1.0–5.0 Gy. Potten (1985) has shown a dose-dependent reduction in hair diameter in mouse guard hairs following ^{137}Cs γ-irradiation in the dose range 0.5–5.0 Gy. Sieber and Wells (1986) and Sieber et al (1987) reported a similar linear response for actively growing pig hair following 250 kV X-irradiation. As in man, control values were negative since hairs become thinner as they emerge from the follicle. The percentage reduction in hair diameter was remarkably similar for the two species with a 6% reduction in diameter per Gy exposure. An exposure to > 5 Gy produced a 30% mean reduction in hair diameter. When the diameter was reduced by $\simeq 50\%$ the hairs broke and were lost from the study. This marks the upper limit of sensitivity of the test. Epilation following irradiation is a recognized phenomenon. It is dose dependent over the range 5.0–14.0 Gy in the pig (Sieber & Hopewell, 1990). Hair loss was assessed with an arbitrary visual scoring system and quantified (Sieber & Hopewell, 1990). It could be measured 14 days post-irradiation, and maximum hair loss was observed at 6 weeks. Although epilation following radiotherapy and chemotherapy is a recognized phenomenon, it has not been studied extensively but is part of a continuing study.

All the hairs that had grown in the irradiation field 5–7 days after irradiation were measured. Hair growth is asynchronous in man and the technique used selected out actively growing hairs. It is possible that the radiosensitivity of this selected population is unrepresentative of all hairs. However, the actively growing hairs can be readily identified and it is likely that actively growing hairs would be a more sensitive target than quiescent hairs.

Radiation damage to the matrix cells of actively growing hairs resulted in a permanent and measurable reduction in hair diameter, which could provide information on the distribution of dose following accidental exposure to radiation. A reduction in the diameter of human hairs was measurable over the range of doses studied (3.0–14.0 Gy). The data are restricted by the small number of patients who were prescribed a single dose or fractionated therapy with intervals between each fraction of > 4 days. In addition, many of the patients who met these criteria did not have suitable hair in the radiation field. The large error associated with some of the data points was due to the small number of hairs within the radiation field. There was a measurable reduction in hair diameter following radiation and the response did appear to be relatively consistent for a variety of commonly used radiation modalities given the limited amount of data available. It is not possible to make any conclusions about differences in the reduction in hair diameter between hairs collected from different body sites. No obvious differences were observed from the limited data available (Table I). Using the regression line drawn through the data points so far available, the percentage reduction in diameter for human hair is of the order of 2.4% per Gy exposure.

The results suggest that human hairs are less sensitive to radiation than mouse/pig hairs. Although there appears to be a dose–effect relationship the data at present are insufficient to determine the nature of the relationship, particularly at low doses, and further studies are needed to establish this. The data available cover the limited range of prescribed doses. At present it is not possible to say whether measurement of the reduction in hair diameter will have a role in biological dosimetry The range of doses (3–14 Gy) of the data presented here might be useful in an accident situation, particularly where a non-uniform overexposure occurred.

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The influence of methotrexate on radiation-induced damage to different lengths of the rat spinal cord

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Abstract. An experimental model in the rat has been used to assess the possible enhancement of damage to the spinal cord when radiation is given in the presence of methotrexate (MTX). The dose of MTX used, 4 mg/kg, was the maximum dose that could be given to the rat, when administered into the cerebral spinal fluid circulation, without risk of serious neurological effects. Lengths of 4, 8 and 16 mm of the cervical spine were irradiated with single doses of X rays. For animals that developed paralysis within 30 weeks, caused predominantly by the presence of white matter necrosis, there was no evidence to indicate that MTX enhanced the radiation response of the rat spinal cord, at least at a more clinically relevant level of effect *i.e.* a low incidence of paralysis. However, for the doses associated with the 50% level of effect (ED_{50}) to an 8 mm long field a significant ($p < 0.005$) enhancement of the response was seen, suggesting a dose modification factor of 1.19 ± 0.07. This was interpreted in terms of an hypothesis to explain the well documented volume effect for very small fields in the rat spinal cord which is based on the migration of viable cells in the periphery of the irradiated site. The apparent smaller effect seen when only 4 mm of the spine was irradiated might be related to the nature of the lesion induced at doses required to produce paralysis in these small fields; the lesions were not restricted to white matter but were more severe and also involved the grey matter and nerve roots after a slightly shorter latent period.

The prophylactic irradiation of the central nervous system (CNS) in combination with intrathecally administered methotrexate (MTX) has proved to be highly effective in the treatment of leukaemia; preventing CNS relapse and prolonging complete remission (Pinkel et al, 1977; Schweinle & Alperin, 1980). However, neurological complications involving the brain and spinal cord have been reported (Luddy & Gilman, 1973; Gagliano & Costanzi, 1976). Usually these complications are transient, but cases of permanent late sequelae have been reported including sensory paraparesis and death. The histological picture of necrosis in the white matter or vascular damage is indicative of radiation injury. However, there have been reports of severe myelopathy after intrathecal MTX alone (Clark et al, 1982) and hence the role played by either agent is uncertain.

In the present communication a well established rat model (van der Kogel, 1979) has been used to assess further the possible modification of the radiosensitivity of the spinal cord by MTX. In an earlier study it has been demonstrated that the maximally tolerated dose of MTX had no effect on the radiosensitivity of the rat spinal cord for either the early delayed or the late delayed lesion (van der Kogel & Sissingh, 1985). However, these studies were carried out after the irradiation of a relatively long length of spinal cord in the rat (15 mm). In a subsequent communication (Hopewell et al, 1987), the results of the effects of radiation of the cervical spine of the rat had indicated that the radiosensitivity of the cord, at least for the early delayed white matter lesion, was highly dependent on the length irradiated. The ED_{50} for the paralysis resulting from this lesion increased from about 21.5 Gy to about 50 Gy when the length of cord exposed was changed from 16 mm to 4 mm. It has been argued that the volume effects for small lengths of spinal cord might be related to the migration of viable cells from the edges of the irradiated volume (Hopewell & van der Kogel, 1988). The purpose of the present study was to examine the effects of MTX on the known volume effect for the rat spinal cord after single doses of irradiation.

Materials and methods

Female rats of the Sprague Dawley strain, 12–14 weeks of age, were used in these investigations. Three different lengths of the cervical spine, 4, 8 and 16 mm, were locally irradiated with a range of single doses of 250 kV X rays, as described previously (Hopewell et al, 1987). Irradiations were carried out with the rats under chloral hydrate anaesthesia (300 mg/kg). Groups of 5–6 animals were irradiated at each dose level for each field size.

At an interval of between 30 and 45 min before irradiation MTX (4 mg/kg–32 mg/m^2) was introduced into the cerebral spinal fluid circulation. This dose of MTX was the maximum tolerated by the rats without acute neurotoxic effects. In a previous pharmacokinetic study (van der Kogel & Sissingh, 1985) peak concentrations of the drug were measured in the rat spinal cord at

30 min after injection. MTX was administered, via the left lateral ventricle, by first "thinning" a small area of the left parietal bone using a dental burr, 2 mm from the midline and 1 mm behind the left coronal suture. The delivery needle was inserted to a depth of 5.5 mm into the left lateral ventricle and MTX (Lederle Laboratories) at a concentration of 25 mg/ml was delivered slowly over approximately 30 s. The initial incision of the overlying skin was sutured.

Following irradiation the animals were housed in cages in groups of 5–6 and fed on a standard laboratory diet (41B) and water *ad libitum*. They were examined at least three times per week to determine the first appearance of neurological signs that might progress to paralysis. Animals that developed paralysis within 30 weeks of irradiation were perfusion fixed under light ether anaesthesia using a mixture of 10% formal saline with 1% acetic acid. Following fixation the cervical and upper thoracic spine containing the irradiated section was decalcified in 8% formic acid for 10 days. 2 mm thick transverse sections of the irradiated length were then taken, they were dehydrated and embedded in paraffin wax. Sections were cut at 5 μm and these were stained with either Mayer's haematoxylin and eosin or Luxol Fast Blue PAS.

All data are expressed as the mean of the individual values, plus or minus one standard error (±SE). Student's *t*-test was used to calculate probability (*p*) values. In all tests a value of $p < 0.05$ was regarded as statistically significant. Dose effect curves were fitted to the data using probit analysis.

Results

The dose-related changes in the incidence of paralysis within 30 weeks in animals irradiated in combination with MTX to 4, 8 and 16 mm of the cervical spinal column are shown in Fig. 1. These results are compared with those for irradiation alone in experiments carried out over the same time period and for which information has already been published (Hopewell et al, 1987). The resulting ED_{50} values (±SE) for both sets of data are listed in Table I. In common with the results for X rays alone the ED_{50} values for paralysis after X irradiation combined with MTX increased as the field size decreased. For the largest 16 mm field the dose-effect curves for the incidence of paralysis were very similar with identical ED_{50} values of 21.5 Gy. When an 8 mm length of the cervical spine was irradiated the dose-effect for the group receiving MTX was shifted to the left and was significantly steeper ($p < 0.001$) than that for X rays alone. The resulting ED_{50} values (±SE) of 25.3±0.7 Gy and 30.1±1.5 Gy were significantly different from each other ($p < 0.005$), suggesting a modification factor of 1.19±0.07. There was also a small shift in the dose-response relationship for paralysis in animals irradiated to 4 mm of the spinal cord in combination with MTX, the dose-effect curve having a similar slope to that for X rays alone. The dose modification factor of 1.07±0.07 was not significant ($p > 0.2$).

Table I. Variation in ED_{50} values (±SE) for animals developing paralysis with 30 weeks of X irradiation alone or a combination of MTX and X rays to the spinal cord of rats

Field size (mm)	Treatment schedule	ED_{50}±SE (Gy)
16	X rays	21.5±0.3
	MTX+X rays	21.5±0.4
8	X rays	30.1±1.5
	MTX+X rays	25.3±0.7
4	X rays	51.0±2.3
	MTX+X rays	47.5±2.1

The latency times for the development of paralysis within 30 weeks for animals irradiated in combination

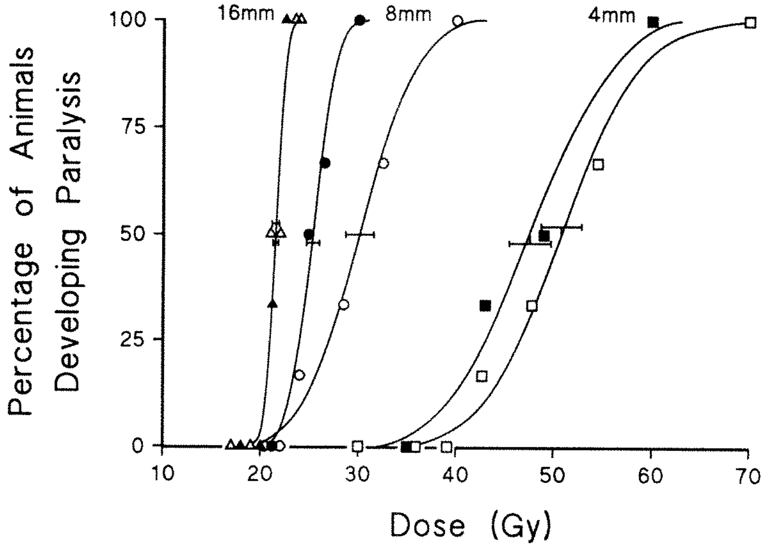

Figure 1. Dose-related changes in the proportion of animals developing paralysis within 30 weeks of the irradiation of 4 (□,■), 8 (○,●) and 16 mm (△,▲) lengths of the spinal cord of rats with single doses of X rays. Previous data (Hopewell et al, 1987) for irradiation given alone (□,○,△) is compared with that for irradiation in combination with MTX (■,●,▲). Error bars indicate ±SE.

with MTX as compared with X rays alone are shown in Fig. 2. Values for the latency time are only shown in dose groups where at least two animals developed paralysis. Some animals treated with X rays in combination with MTX did not develop paralysis within 30 weeks. Some of these animals, in line with the X ray alone groups, did show neurological damage after latent periods > 45 weeks. However, external unrelated factors prevented a systematic evaluation of animals surviving for > 30 weeks.

There were no major differences in the latency for paralysis between animals receiving local cord irradiation and those irradiated in combination with MTX. Although there was not a clear distinction, the latent period for paralysis in animals receiving irradiation to 4 mm of spinal cord tended to be slightly shorter than that for the two larger fields; doses of at least 40 Gy were required to induce a response. A notable exception was the group of five rats irradiated to 8 mm of cord with a single dose of 40 Gy alone. All five animals developed paralysis after an average latency of 20.9 ± 0.6 weeks. The dose associated with the same incidence of animals developing paralysis in the combined treatment was 30 Gy where the mean latency was significantly longer at 25.5 ± 0.7 weeks ($p < 0.001$).

After the irradiation of 4 mm of spinal cord with doses necessary to produce paralysis, degeneration of grey matter and demyelination of the nerve roots were seen in addition to the more characteristic white matter lesions. This applied equally to the groups receiving irradiation alone or the combined treatment. Selective white matter necrosis was usually characteristic of animals irradiated to 8 and 16 mm of the spinal cord.

Discussion

MTX is a folic acid antagonist and as such it has an inhibitory effect on DNA synthesis. Therefore, populations of cells that are cycling tend to accumulate in the G_1–S transition phase of the cell cycle after MTX administration (Chabner & Young, 1973). This could explain the observed enhancement of the radiation response by a similar dose of 4 mg/kg of MTX, given

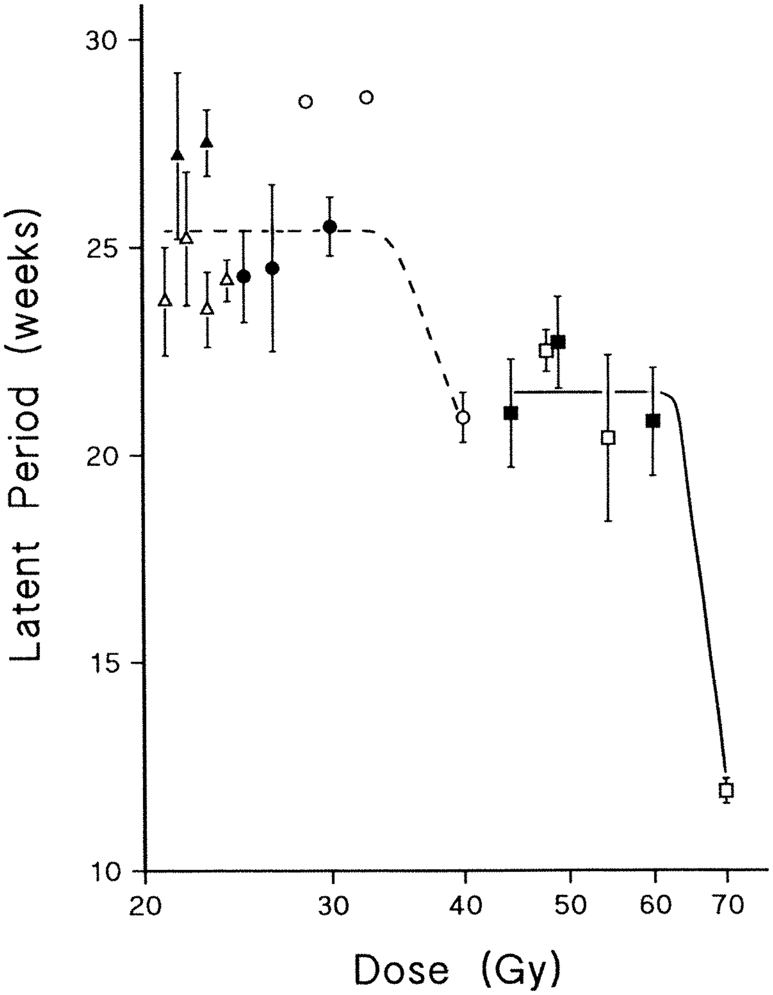

Figure 2. Dose-related changes in the mean latency for the development of paralysis within 30 weeks of the irradiation of 4, 8 or 16 mm of the spinal cord of rats with single doses of X rays. Data points are only plotted for doses at which 2 animals in the group developed paralysis (for keys to symbols see Fig. 1).

into the lateral ventricles, on the neuroglia stem cell population in the subependymal region of the rat brain (Morris & Hopewell, 1983). However, the possibility of a simple additivity of the cytotoxic effects of the two agents could not be excluded.

In the spinal cord of the adult rat there is no relatively rapid proliferating neuroglial stem cell population and the dose of MTX used in the present study was, on the basis of a pilot investigation, the maximum that could be given to the rat without evidence of acute neurological damage. This dose produced no apparent long-term effects. The similarity of the dose-effect curves for the incidence of paralysis for irradiation alone or in combination with MTX to 16 mm of the spinal cord, supports the view that in this slowly proliferating cell system MTX at the dose used produced no enhancement or evidence for additive cytotoxicity in the spinal cord. This supports earlier findings (van der Kogel & Sissingh, 1985) in the rat when similar field sizes were used. However, it should be remembered that very high doses of MTX, when administered alone to patients, have resulted in a demonstrable cytotoxic effect on the CNS (Skullerud & Halvorsen, 1978; Clark et al, 1982). It cannot be ruled out that lower doses of drug may produce generalized subclinical damage in the CNS.

Given that there was no obvious modification in the radiation response when 16 mm of the spinal cord was irradiated, it was somewhat of a surprise to see a marked modification in the effect when only 8 mm of the cord was exposed. The resulting dose-effect curve for the combined treatment was steeper than for radiation alone. The implications of this change are a large dose modification factor (DMF) at a high level of incidence of paralysis (DMF > 1.2) declining to insignificantly small values at more clinically relevant levels of effect. (< ED_5). This would suggest that MTX is unlikely to enhance the radiation-induced response in the spinal cord even in small high dose regions where treatment volumes overlap. The most likely explanation of these findings is that MTX does indeed produce subclinical injury to the CNS and that the migration of cells from the periphery of the 8 mm long irradiated site is in some way inhibited. This results in an enhancement of the radiation effect in that volume. The response of longer lengths of the spinal cord ($\geqslant$ 16 mm) would not be affected in this way, since other studies (van der Kogel, 1991) have suggested that ~ 10 mm is the maximum length over which cell migration might exert an effect in modifying the late radiation response of the spinal cord. The possible effects of MTX in inhibiting or reducing cell migration are supported by more recent irradiation studies (van der Kogel, unpublished). In these studies a small length of the spinal cord (4 mm) was irradiated within a larger area (18 mm) that had received a sub-threshold dose. There was a significant reduction in the ED_{50} for paralysis within 30 weeks, from 45 Gy to 27.5 Gy, indicating that the sparing of damage usually associated with small volumes had largely disappeared. Although both of these studies provide support for the view that the migration of viable cells from the edges of the irradiated length provides an explanation for the observed volume effect in small fields for the spinal cord, the exact explanation of the observed volume effect still remains uncertain. The migration of viable epithelial cells from the edges of the unirradiated site would appear to explain area effect from acute reactions in pig skin (Hopewell, 1990).

Given the effect of combined treatment with MTX in modifying the response of 8 mm of the spinal cord to radiation, and its possible explanation, a similar if not more marked effect might have been anticipated after the irradiation of 4 mm of the spinal cord. Although the magnitude of the reduction in the ED_{50} for paralysis for the 4 mm and 8 mm fields was similar, 3.5 Gy as compared with 4.8 Gy, the dose-modification factor for the 4 mm fields was not significant and there was no change in the slope of the dose-effect curve. Although this might appear to be a contradictory finding, it may be related to the different nature of the lesion induced at doses required to produce paralysis when only a 4 mm length of the spinal cord is irradiated. The lesions seen were not restricted to the white matter, but are more extensive and also involve the grey matter and the nerve roots. Details of the different histological lesions associated with 4 mm as compared with larger lengths of irradiated cord have been discussed in detail previously (Hopewell et al, 1987). The latency associated with such lesions is also slightly shorter, both for radiation alone and the combined treatment group when compared with that for effects in larger fields. Here again an analogy can be drawn with effects seen in the skin, for fields of < 5 mm diameter; the migration of epithelial cells from the periphery of these sites is such that moist desquamation is avoided and any lesion seen is related to effects in other cell populations, the death of which results in a more severe lesion in a shorter latent interval (Hopewell, 1990).

Thus, in summary, at clinically relevant levels of effect, *i.e.* a low incidence of radiation-induced paralysis, there was no evidence to indicate that MTX enhanced the radiation response of the rat spinal cord. For more severe levels of damage, changes were seen that could be interpreted as indicating that cell migration from the periphery of fields of no more than 8 mm length was a key factor in explaining tissue volume related effects, rather than any model based on the specific arrangement of any theoretical functional sub-units (Withers et al, 1988), the biological identity of which has still to be validated.

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Re-irradiation of soft-tissue sarcoma

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Abstract. Re-irradiation for local recurrence of malignancy after radical radiotherapy is of proven benefit at head and neck sites but has seldom been used elsewhere. This paper reports a series of 10 patients re-irradiated with external-beam techniques for local recurrence of soft-tissue sarcoma of the limb and limb girdle following initial limb conserving management with surgery and radiotherapy (dose range 33–60 Gy). Median survival was 14 months following re-treatment. Two cases received treatment with high-energy electrons and the rest with megavoltage photons. Five patients re-treated with radical intent (dose range 40–60 Gy) had a median survival of 36 months and median recurrence-free survival of 16 months. All five patients treated palliatively (dose range 12–50 Gy) have died, although two demonstrated local control until death. Acute reactions were not severe. Radionecrosis was seen in one patient who was re-irradiated twice (total dose 145 Gy) and subsequently required amputation. One other case required amputation for persistent local disease, but in the remaining eight, limb conservation was achieved. Re-irradiation of soft-tissue offers good local control and may avoid amputation.

In the treatment of soft-tissue sarcoma of the limb and limb girdle, 5-year local control rates of 80–90% have been achieved in a number of centres (Suit et al, 1988; Robinson et al, 1990) using a combination of limb conserving surgery and high-dose radiotherapy. For patients with high-grade tumours that fail locally, the outlook is poor with a high probability of metastatic disease; local control remains a major objective, without resort to ablative surgery. Similarly, for patients with recurrent low-grade tumours, further surgical treatment is likely to entail amputation. Re-irradiation offers an alternative approach for both categories of patients. Although the cumulative radiation dose will exceed conventional tissue tolerance, both experimental studies and practical experience have shown re-irradiation to be a feasible proposition, without excessive rates of tissue necrosis.

In head and neck cancer, re-irradiation after prior radical dose radiotherapy has been reported by a number of centres and appears to give acceptable local control (Wang & Schulz, 1966; Kumar et al, 1978; Nisar Syed et al, 1978; McNeese & Fletcher, 1981; Emami et al, 1987). Fast neutrons have been used to re-treat a small number of patients with recurrent sarcoma (Saroja et al, 1988). There is no previous report on the use of external-beam radiotherapy with photons for the re-irradiation of soft-tissue sarcoma of the limb or limb girdle, where field sizes are generally large. This paper reports a series of 10 patients who were re-irradiated for locally recurrent sarcoma.

Materials and methods

Between 1981 and 1987, 10 patients (four male and six female) with recurrent soft-tissue sarcoma of the limb and limb girdle were re-irradiated following initial limb conserving treatment with surgery and radiotherapy in eight and surgery alone in two. The mean age of the patients was 53 years. Tumour histology has been reviewed and was: liposarcoma (5), fibrosarcoma (2), malignant fibrous histiocytoma (1), pleomorphic rhabdomyosarcoma (1) and synovial sarcoma (1). Six tumours were high grade and four were low grade. Where the original diagnosis was made at another institution, full details have been obtained and histology reviewed. Table I details patient characteristics and histology. Cases 4, 9 and 10 were treated by surgery alone at initial presentation. The first course of radiotherapy was given as part of the treatment for first local recurrence in Cases 9 and 10, second local recurrence in Case 4 and as part of initial therapy in the remainder. One patient was treated with high-energy electrons, one with orthovoltage X-rays (in 1958) and the remainder with megavoltage photons. Five patients received their initial radiotherapy at another centre.

Details of the Royal Marsden Hospital Sarcoma Unit treatment policies for extremity sarcomas have been published previously (Robinson et al, 1990). Radical radiotherapy is usually given post-operatively in two phases. The first phase treats the volume considered to be at risk of microscopic spread. Where tumour is intracompartmental this involves treating the whole muscle compartment to 50 Gy in daily 2 Gy fractions over 5 weeks. A strip of normal tissue is spared along the length of the irradiated limb, and joints are spared whenever possible. The second phase treats the tumour bed and scar with a 2 cm margin to a total dose of 60 Gy in 30 fractions over 6 weeks. All fields are simulated and tissue compensators used where necessary.

The mean field length used for re-treatment was 18.6 cm (range 10.5–28 cm) given as a single-phase treatment. Two patients were re-treated with high-energy electrons and the remainder with megavoltage photons.

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Table I. Patient characteristics at presentation

Case	Sex	Age (years)	Histology	Grade	Site	Size (cm)	Surgery at presentation
1	F	56	Myxoid liposarcoma	Low	Buttock	N/A	Biopsy
2	F	50	Synovial sarcoma	High	Upper arm	4 × 4	Marginal excision
3	F	47	Liposarcoma	High	Upper arm	8 × 6	Compartmental resection
4	F	33	Fibrosarcoma	Low	Lower leg	N/A	Wide excision
5	M	57	Myxoid liposarcoma	Low	Lower leg	6 × 1.5	Marginal excision
6	F	60	Rhabdomyosarcoma	High	Thigh	6 × 6	Biopsy
7	F	63	Pleomorphic liposarcoma	High	Lower leg	10 × 6.5	Marginal excision
8	M	79	Liposarcoma	High	Lower leg	25 × 19	Biopsy
9	M	38	Fibrosarcoma	Low	Thigh	1 × 1.5	Marginal excision
10	M	46	Malignant fibrous histiocytoma	High	Thigh	8 × 8	Marginal excision

N/A = not available.

Because of variations in dose per fraction used in these patients, regimes were compared using the FDF method (Thames & Hendry, 1987). This is derived from the linear-quadratic model and may be considered applicable to late-responding normal tissues, when the effect of overall treatment time can be ignored. An α/β ratio of 3 Gy^2 was used to calculate the total effect (TE) = $(\alpha/\beta + d) \times D$, where d is the dose per fraction and D the total dose given.

Cases 1–5, with locally recurrent disease but no evidence of metastasis at re-staging, were treated with radical intent using a combination of surgery and radiotherapy. The details of treatment, including TE values, are given in Table II. The remaining five cases received palliative re-irradiation for recurrent disease either because of inoperable disease previously treated with radiotherapy alone, or because of the presence of metastases.

Results

The median actuarial survival for the entire group was 14 months from the date of completing treatment for recurrence (Fig. 1).

Those patients treated with radical intent (Cases 1–5) received a mean TE of 392 Gy^2 (dose range 40–60 Gy). Median survival was 36 months and local control was achieved for a median time of 16 months (Fig. 2). One patient (Case 2) died from metastatic disease with no evidence of further local recurrence. One patient (Case 5) underwent a second radical re-treatment with surgery and radiotherapy in an attempt to avoid amputation following further local recurrence. He received a total

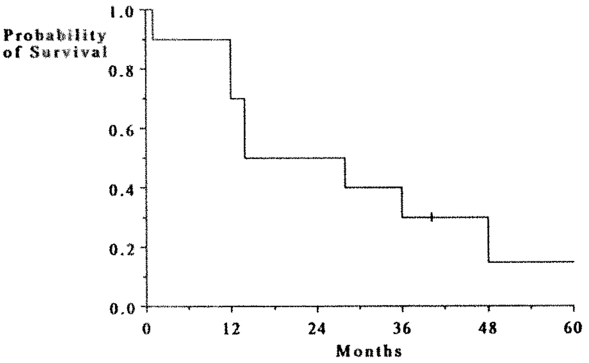
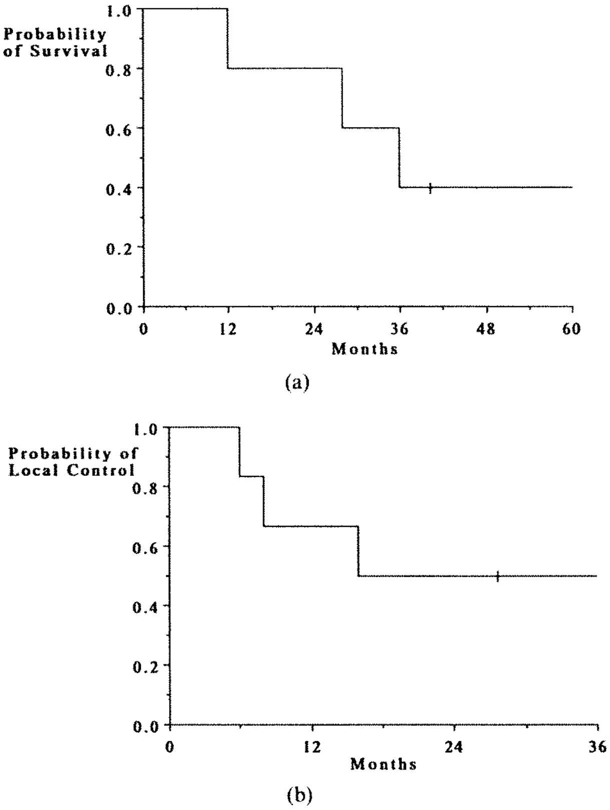


Figure 1. Actuarial survival: all patients.



(a)

(b)

Figure 2. (a) Acturial survival: radical treatment group. (b) Acturial local control: radical treatment group.

Table II. Treatment details

Initial Treatment				Treatment Relapse						
Case	Surgery	Radiotherapy	TE	DFI	Surgery	Meta-stases	Radiotherapy	TE	Field size (cm)	Status at follow-up
1	Biopsy	54 Gy/18f/6 weeks	324	24	Wide excision	No	60 Gy/30f/6 weeks	300	15.5 × 7.5	LR 17 months Died 36 months LR & mestastases
2	Marginal excision	40 Gy/9f/4 weeks	298	324	Wide excision	No	60 Gy/30f/6 weeks	300	28 × 9	Died metastases 28 months No LR
3	Compartmental resection	60 Gy/30f/6 weeks	300	8	Marginal excision	No	36 Gy/18f/4 weeks	180	15 × 8	LR 7 months Died metastases 13 months
4	Wide excision	33 Gy/10f/3 weeks	208	56	Wide excision	No	39.6 Gy/22f/5 weeks	190	17 × 8.5	Metastasis 33 months No LR 40 months
5	Marginal excision	46 Gy/7f/6 weeks	440	15	Wide excision	No	39.6 Gy/6f/5 weeks	380	12.5 × 9	LR 9 months
				9	Wide excision	No	60 Gy/30f/6 weeks	300	27 × 9.5	Amputation 61 months NED 105 months
6	Biopsy	33 Gy/6f/6 weeks	280	8	Biopsy	No	33 Gy/5f/4 weeks	317	18 × 14	LR 8 months
				8	Biopsy	Yes	26 Gy/4f/3 weeks	247	21 × 15	Died 7 months LR & metastases
7	Marginal excision	56 Gy/16f/5.5 weeks	364	31	Biopsy	No	20 Gy/10f/2 weeks	100	16.5 × 10	LR 10 months Died 48 months LR & metastases
8	Biopsy	50 Gy/25f/5 weeks	250	12	None	Yes	12 Gy/2f/1 week	70	23 × 18	Died 1 month LR & metastases
9	Marginal excision	40 Gy/25f/5 weeks	184	20	Biopsy	Yes	40 Gy/20f/4 weeks	200	16 × 8	Died 14 months metastases No LR
10	Marginal excision	60 Gy/30f/6 weeks	300	13	Biopsy	Yes	50 Gy/20f/4 weeks	275	10.5 × 10	Died 12 months metastases No LR

DFI = disease-free interval to local recurrence in months; LR = local recurrence; NED = no evidence of disease; TE = total effect (Thames & Hendry, 1987).

dose to the lower limb of 145 Gy over a 24 month period. Local control was achieved with no loss of function or excess acute toxicity. Amputation was subsequently required for radionecrosis which developed after trauma 61 months following completion of the final treatment.

Those patients treated with palliative irradiation received a mean TE of 321 Gy^2 (dose range 12–50 Gy). Case 7 required amputation for local recurrence after low-dose re-irradiation but subsequently died with both local and distant disease. The remaining four patients had large inoperable tumours and have all died from metastases. Two of these (Cases 9 and 10) achieved local control with re-irradiation.

Re-treatment was well tolerated in both groups despite the relatively large field sizes used. Acute and late reactions were scored mild, moderate and severe. Acute radiation reactions were severe in two cases (with moist desquamation that healed with conservative treatment) and moderate in one case. Late radiation reactions were severe in one case (with radionecrosis as noted above) and moderate in two (with oedema and diminished limb function).

Discussion

The tolerance of tissues to re-irradiation has not been extensively studied. The results of Hendry et al (1977) on mouse and rat tails showed only a 10% reduction in late normal-tissue tolerance to radical re-irradiation 6 months after a previous radical dose. Brown and Probert (1975) compared early and late reactions on the mouse leg and found very little memory for acute skin reactions, whereas late deformity did show a cumulative effect. However, Simmonds et al (1989) could find no evidence of residual injury to pig dermal tissue following re-irradiation at various times after a tolerance dose of photon irradiation. The tolerance of human skin to re-irradiation was shown in a small series of patients radically irradiated for hypopharyngeal tumours 5–50 years after neck radiotherapy (Hunter & Stewart, 1977). All had normal acute skin reactions despite re-treatment through skin showing late radiation sequelae of atrophy and telangiectasia.

The largest reported clinical experience of re-irradiation is at head and neck sites. Both external-beam and brachytherapy have been used rendering interpretation of results and assessment of tolerance difficult because of the wide variation in dose and volume treated. Acute radiation reactions are generally within normal limits. Late necrosis rates from a number of series vary from 2% to 30% (Nisar Syed et al, 1978; Skolyszewski et al, 1980; McNeese & Fletcher, 1981; Langlois et al, 1985; Errington & Catterall, 1986; Emami et al, 1987; Pomp et al, 1988; Skolyszewski & Korzeniowski, 1988; Sham et al, 1989), with the higher values described predominantly with brachytherapy. The present series similarly confirms the minimal acute toxicity of re-irradiation. The present data do not allow any firm conclusions to be drawn on late radiation tolerance because of the short follow-up; however, there do not appear to be any significant problems with cumulative doses up to 100 Gy at 2 Gy daily.

In re-treatment studies of head and neck cancer using external-beam radiotherapy, better rates of local control have been achieved with a combination of surgery and radiotherapy than with radiotherapy alone. The total dose of second irradiation also appears to be important. Pomp et al (1988) showed local control rates of 48% with doses > 50 Gy versus 20% with doses < 50 Gy. Emami et al (1987) in a large series reported that patients receiving > 50 Gy had an 80% complete response rate and 25% eventual control rate compared with 44% and 11%, respectively, for those receiving < 50 Gy. In the present series a higher total dose also appears to confer greater local control, although the dose given was closely related to treatment intent (either radical or palliative). The effect of such patient selection cannot be excluded from other series and renders interpretation of a dose–response effect difficult.

This series suggests that in a favourable prognostic group of patients with recurrent sarcoma, repeat treatment with conservation surgery and re-irradiation can achieve good local control while preserving limb function. In the palliative group the aim was to delay local tumour progression and this was generally successful. Re-irradiation is both feasible and effective as part of a conservative approach to the treatment of recurrent soft-tissue sarcoma of the limb and limb girdle.

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Minimizing radiation dose to patient and staff during fluoroscopic, nasoenteral tube insertions

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Abstract. It is possible to reduce greatly fluoroscopic radiation dose if some image degradation is acceptable. Since the fluoroscopic image during nasoenteral tube placements is used for guidance and not for diagnosis, a lower contrast image with increased quantum mottle can be easily tolerated. The three methods to reduce the radiation dose rate that were investigated consisted of removing the antiscatter grid, increasing the diameter of the optical aperture controlling the percentage of light reaching the television camera from the image intensifier output phosphor, and setting the fluoroscopic mA to the minimum value so that the kVp could be maximized. Fluoroscopic frozen video frames of a clinical tube insertion comparing the images with and without the dose-saving techniques are presented. Measurements of the radiation dose rates using a Plexiglas phantom show that the dose for patient and staff during fluoroscopic-guided nasoenteral tube placements can be reduced by over a factor of 10 without significantly adversely affecting the actual placement procedure.

The importance of maintaining adequate nutrition as part of the therapeutic regimen in the intensive care unit (ICU), trauma and post-surgical patient has been well documented (Abbott et al, 1987; Alexander et al, 1980; Border et al, 1987; Boucek, 1984; Kudsk et al, 1982; Mullen et al, 1980; Ruberg, 1984). Thus placement of enteric feeding tubes into the proximal jejunum is undertaken routinely with fluoroscopic guidance (Gianturco, 1967; Sax & Hurst, 1987; Shipps et al, 1979). However, the serpiginous anatomy of the proximal gastrointestinal tract combined with the poor physical condition of the critical care patient often warrant lengthy attempts at adequate tube positioning, even with the use of fluoroscopy. Potentially long exposure times, estimated by one author (Shipps et al, 1979) to be up to 10 min, can result in significant radiation hazards when considering that multiple procedures may be required, owing to inadvertent tube clogging or extraction, during the hospitalization of a single individual. At one of the authors' affiliated hospitals it was found (Rudin et al, 1991a) that more than half of the procedures are performed on patients who have undergone prior enteric tube placements during the course of the same hospitalization.

To minimize dose to both staff and patient, general principles of radiation protection (Cember, 1969) using time, distance and shielding should be applied whenever possible. Since the patient must be imaged by direct exposure to radiation, the latter two factors may not always be applicable for patient dose control. Furthermore, because the fluoroscopic exposure time depends on the progress of the procedure, it may not be possible to control the exposure time. For staff involved in the procedure, increasing the distance from the patient, the source of scattered radiation, may be difficult. Shielding staff from scattered radiation using lead aprons and curtains should always be attempted. However, for those required to be in close contact with the patient, curtains may be impractical at times.

The authors have been exploring other methods that are based on the fact that significant dose reduction can be gained by alteration of fluoroscopic parameters if limited image degradation is acceptable. The basic premise for the proposed techniques is that the fluoroscopic image during placement procedures is not used for disease diagnosis and, therefore, need not be of the highest quality. The image simply must be of sufficient quality for detecting the position of the nasogastric tube's metal tip, which is highly radio-opaque, relative to the anatomy.

The authors (Rudin et al, 1991a) have previously used the techniques of antiscatter grid removal and increased optical video aperture to reduce the radiation dose rate while degrading image quality. By removing the grid (Gray & Swee, 1982) and accepting scattered photons, dose reduction with some decreased image contrast occurs. By increasing the size of the optical aperture normally placed between the output phosphor of the image intensifier (II) and the input to the TV camera, more light is allowed to reach the TV camera per X-ray photon absorbed in the II, and thus fewer X-ray photons are needed. Fewer photons implies lower radiation exposure but also greater quantum mottle or noise in the image. The authors (Bednarek et al, 1983a, b) and others (Leibovic & Caldicott, 1983; Rossi et al, 1978) have used this principle in reducing dose for other radiological procedures.

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A third method of dose reduction introduced here involves the use of increased kilovoltage (kVp) settings with the automatic brightness control (ABC) system of the fluoroscopic unit. The ABC system normally changes both the kVp and mA of the X-ray generator dynamically and automatically so that the light level at the TV camera is maintained constant, independent of changes in patient attenuation. By setting the mA to the minimum value instead of to an automatically adjusted value, the ABC will change the kVp to a higher than normal value resulting in X rays having increased penetrability. A lower X-ray output is thus needed to maintain the same brightness at the input to the TV and dose rate can be significantly reduced. The concomitant effect of the use of higher-energy photons is a reduction in image contrast and slightly increased noise owing to the use of fewer photons.

In the following, estimates of the dose reduction to patients and staff by the use of combinations of these three methods are reported.

Materials and methods

Exposure measurements were made for each technique using a 20 cm thick 12 in × 12 in acrylic phantom, which was supported 2 cm above the table top of a fixed, undertable tube fluoroscopic unit (Philips Model Diagnost 73) with the bottom of the II tower housing touching the top of the phantom. A pancake-shaped ionization chamber (Keithley Model 96035) was placed on the table surface under the phantom, and the entrance surface exposure was determined using a dosemeter (Keithley Model 35050) with a digital multimeter (Fluke Model 8050A). The exposure rate measurements were multiplied by the mean fluoroscopic exposure times and by an exposure to a dose conversion factor (Meredith & Massey, 1977) for muscle of 0.92 cGy/R to determine the mean patient entrance dose per procedure.

Scattered radiation exposure measurements were made at 20 cm and 40 cm from the centre of the phantom, which was located at the centre of the X-ray field. A portable ionization chamber survey meter (Victoreen Model 450) with manufacturer's specified accuracy of 10% was used for these measurements. The 10 : 1 ratio grid's position "in" or "out" of the beam was motor driven and controllable by the operator. The optical aperture size was changed between 46.5 mm (large) and 20 mm (small) using a solenoid driven device (Philips Model 4535–220–48321 Auto Diaphragm Type 9807-0510-1170). The ABC was adjusted simply by turning the manual mA adjustment potentiometer accessible to the operator under a retractable panel on the fluoroscopic unit spot film housing. The potentiometer was turned only enough to remove it from the automatic detente so that it was forced to be minimum while the kVp potentiometer was left on the automatic detente.

In order to illustrate the effect of fluoroscopic parameter alteration to minimize dose on image quality, a patient study was videotaped using a SONY U-Matic Model 5600 VCR. Corresponding images from the tape for normal and reduced dose settings were frozen with a frame-freeze device (Rudin et al, 1991b) and hard copy of these frozen images was made using a Matrix camera (Model 1010-2).

Results

Table I gives the results of exposure measurements for the 20 cm plastic phantom. The measurement repro-

Table I. Expected patient entrance surface dose per procedure and scattered radiation to staff measured for different fluoroscopic parameters using a 20 cm Plexiglas phantom

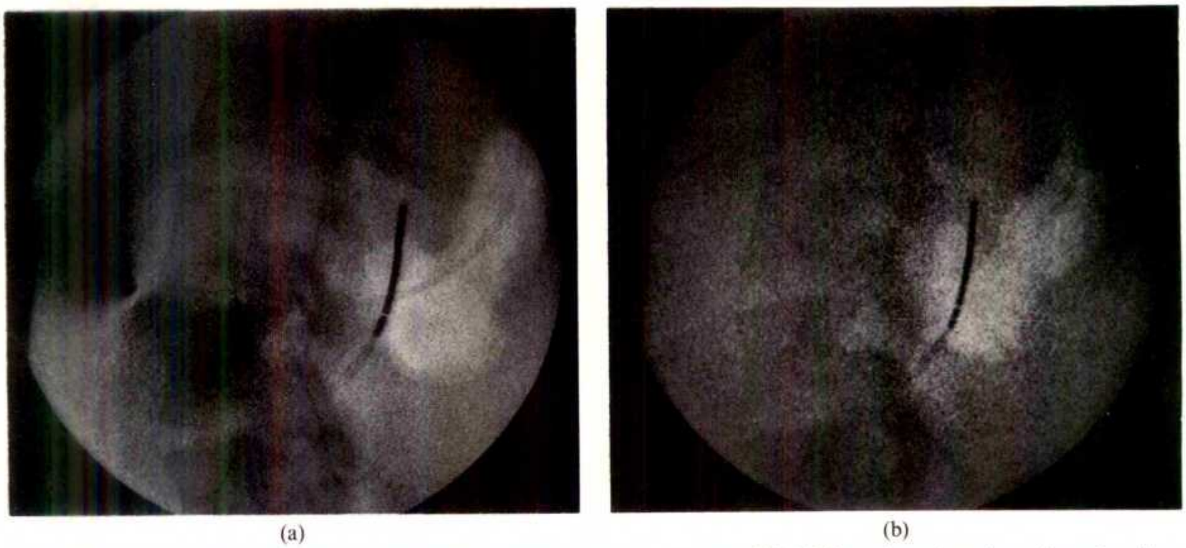
	Set of conditions						
	A	B	C	D	E	F	G
kVp	83	71	65	110	105	59	70
mA	2.8	2.2	1.8	min*	min*	1.4	min*
Grid	In	Out	In	In	Out	Out	Out
Optical aperture	Small	Small	Large	Small	Small	Large	Large
Entrance exposure rate (R/min)[a]	5.55	2.93	2.04	1.40	1.25	1.14	0.51
Expected mean patient entrance dose per procedure (cGy)	24	13	8.8	6.1	5.4	4.9	2.2
Patient dose reduction factor[c]	1.0	1.9	2.7	4.0	4.4	4.9	10.9
Scatter exposure:							
At 20 cm (mR/h)[b]	1300	580	340	470	400	150	105
Reduction factor[c]	1.0	2.2	3.8	2.8	3.3	8.7	12.4
At 40 cm (mR/h)[b]	330	145	92	110	98	40	25
Reduction factor[c]	1.0	2.3	3.6	3.0	3.4	8.3	13.2

* Approximately 0.3 mA.

[a] Multiply table entries by 2.58×10^{-4} to obtain exposure rate in C/ (kg min).

[b] Multiply table entries by 2.58×10^{-4} to obtain exposure rate in mC/ (kg h).

[c] Relative to value in column A.



(a) (b)

Figure 1. Digital video frame of the final placement of a feeding tube in a 29-year-old, 177 lb, male patient whose dimension along the central beam was measured to be 20.5 cm. (a) Standard ABC settings resulting in 2.7 mA and 80 kVp, "normal" small-aperture setting, with grid in place, and (b) ABC set so mA is minimum resulting in 70–75 kVp, "low dose" large-aperture setting, with grid withdrawn. The kVp decreased owing to a reduced demand for X-ray fluence with the larger aperture and the grid removed.

ducibility was about 2% owing to the variation in X-ray generator output. Each column denotes a different set of fluoroscopic parameters as indicated in the first four rows for kVp, mA, grid status and optical aperture status. The columns are arranged in order of decreasing entrance exposure rate (fifth row) and expected patient entrance dose per procedure (sixth row) calculated using the mean times of 282 s (4.7 min) for 148 clinical procedures surveyed. The dose reduction factor (seventh row) is thus in order of increasing value. The final four rows indicate the scatter exposure rate at 20 cm and 40 cm from the centre of the X-ray field along with scatter exposure-rate reduction factors of each set of conditions relative to that of column A.

Figure 1(a, b) demonstrates the comparison between images obtained with normal and dose-minimized parameters from the same patient study.

Discussion

The expected patient entrance dose per procedure given in Table I was calculated using the mean exposure time; however, exposure times for individuals can be significantly larger than the mean and, as stated previously, individuals can receive numerous procedures during a hospital stay. Patient dose values in tens of cGy may be considered among the highest of common radiological procedures.

The values of radiation dose reduction factor for each set of conditions from columns B through G in Table I are given relative to the set of conditions in column A, which represents a fluoroscopic unit used with none of the three dose reduction methods in force. The three columns marked B, C and D represent the results for each of the three methods used individually, *i.e.* only the grid was removed for set B, only the optical aperture was enlarged for set C, and only the fluoroscopic mA was set to minimum for set D. Clearly, when each of these methods is used individually, setting the mA to minimum has the greatest effect because of the dramatic increase in kVp. When the grid is removed in addition to setting the mA to minimum (column E), only a small additional gain in dose reduction occurs since the kVp decreases. Furthermore, the grid is somewhat less effective in reducing scatter and absorbing primary radiation at higher kVp, and therefore its removal when the mA is minimized (going from column D to E) does not provide as large a dose-reduction factor as at the lower energies when the mA is higher (going from column A to B).

The conditions of column F represent a combination of the grid removed, as in column B, with the aperture enlarged, as in column C. The total reduction factor of 4.9 is about 5% less than the product of the individual reduction factors because the ABC system has caused the kVp to be reduced slightly, thus reducing the penetrability of the beam and requiring a slightly greater X-ray fluence rate.

The conditions of column G represent all three of the dose-rate reduction methods being used simultaneously with a resulting total reduction factor of over an order of magnitude. When the minimization of fluoroscopic mA is added to the other two conditions of column F an additional dose-rate reduction factor of more than 2 occurs along with an increase in the fluoroscopic kVp.

The scatter measurements for the plastic phantom are given at the bottom of Table I and are similar to those of others (Faulkner & Moores, 1982; Trout & Kelly,

1972) taking into account differences in the phantom dimensions. The data may be used to give a rough estimate of the entrance dose to personnel. The value of 40 cm is approximately the distance of the position of the fluoroscopist's hands near the patient's nose during tube insertion. The four times larger exposure rates measured at 20 cm and at the height of the table top can be considered an estimate of the entrance dose to the torso of unshielded personnel in close proximity to the patient near the X-ray field. However, the recommended use of lead curtains or aprons would reduce this considerably.

As expected, the ratio of scatter to entrance exposure rates listed in Table I generally increases with increasing kVp. Thus the differences between the scatter reduction factors and the patient dose reduction factors for the same conditions appear to follow with relative change in kVp; *i.e.* at a kVp higher than the reference kVp of column A the scatter reduction factor is lower and for lower kVp it is greater. Nevertheless, when all three dose reduction methods are in force, as indicated in column G, the exposure reduction to staff is also greater than an order of magnitude.

In practice the dose reduction expected in a given facility depends on a number of factors that may be different from those used in this study. Aside from the obvious differences in patients, operator technique and experience, and which combination of the dose reduction methods is employed, there may be basic differences in the design of the fluoroscopic unit used. For example, use of a 6 in diameter II rather than the 9 in II used in this study would significantly reduce scattered dose and integral patient dose while probably somewhat increasing the patient dose to the area being imaged. Also, if a C-arm were to be used with little or no scatter shielding integral to the unit, then dose to staff could be significantly higher compared with that when using a fixed unit containing curtains and a spot film housing. In addition, the data depend heavily on the ABC tracking curve that the fluoroscopic equipment manufacturer selects for variation of kVp and mA as well as the maximum and minimum mA values available.

The practicality of implementing each of the dose reduction methods also depends on the equipment in question. If the grid is not motor driven, as it was in the case of equipment used in this study, then it might be more inconvenient to remove the grid. For portable C-arm units, however, there is no reason why grids could not be designed to be removed quickly. Similarly, reversible optical aperture variation is a feature that may not be available for some equipment suppliers or may be costly from others, although all suppliers allow manual selection of the iris aperture size when the equipment is first set up. Since motorized variable iris mechanisms are now becoming commonly available on fluoroscopy units used with digital spot film devices, it may be possible to require that manufacturers provide such an option for portable C-arm units for dose reduction purposes. On most units, selection of the fluoroscopic mA and kVp is generally available with panel controls and may, therefore, be the easiest to implement.

Further dose saving might be possible through the use of pulsed fluoroscopy, in which the X-ray beam is pulsed with a low-duty factor yet an image is continuously displayed without flicker through the use of digital image display devices. These techniques, however, can greatly increase the cost of fluoroscopy equipment. Use of a low-dose, low-cost frame-freeze device (Rudin et al, 1991b) rather than spot films for the recording of final tube placements can result in additional dose reduction.

Figure 1 demonstrates the increased quantum noise and reduced quality in a clinical image that results when all three dose reduction methods are implemented. Nevertheless, the image is adequate for guiding the feeding tube to its required final position. For the fluoroscopic equipment at the authors' institution, the operator may reverse any one or all of the dose reduction methods at any time during the procedure if improved image quality is required. In our experience this has not occurred; that it has not implies that the limits on dose reduction have probably not yet been reached.

The present study has dealt only with fluoroscopic feeding-tube placements. These dose reduction methods could in theory be applicable to other procedures such as intravascular catheter placements where reduction in image quality can be acceptable for a significant part of the procedure. However, clinical evaluation of these concepts for such other applications remains to be performed.

Conclusion

This work has reviewed a variety of fluoroscopic equipment and parameter modifications to reduce patient and staff radiation dose. With the continually increasing use of fluoroscopy for critical care patients and with renewed concern over the effects of low doses of ionizing radiation, it seems prudent that all radiological facilities consider implementing as many of these modifications as practicable.

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Technical note

Magnetic resonance imaging of Fricke-doped agarose gels for the visualization of radiotherapy dose distributions in a lung phantom

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When calculating a treatment plan for a radiation beam that passes through an inhomogeneity such as lung, the dose at each point needs to be modified to correct for the effect of the inhomogeneities. Many algorithms exist for making such corrections. Algorithms must be verified by measurements in phantoms. Measurements with an ionization chamber in a solid phantom can only be performed at a limited number of points, giving poor spatial resolution. Film dosimetry gives better spatial resolution, but the introduction of non-tissue equivalent photographic film represents a considerable perturbation of a tissue equivalent phantom.

Shultz et al (1990) and Olsson et al (1990) have recently described techniques for the measurement of absorbed dose using magnetic resonance imaging (MRI) of agarose gels doped with Fricke (iron (II) sulphate) solution. After Fe^{2+} has been oxidized by irradiation to Fe^{3+}, the gel fixes the position of the ions, so that the distribution of Fe^{3+} in the gel corresponds to the dose distribution. The gel is then imaged to produce a map of the longitudinal proton relaxation time (T_1). As a result of the paramagnetic properties of Fe^{3+}, T_1 is inversely proportional to Fe^{3+} concentration and hence to absorbed dose of radiation.

Thus, the technique provides a method of determining a continuous distribution of radiation dose within a phantom. This paper describes preliminary work using the technique on a phantom containing a volume of low density material designed to simulate lung. The measured distribution is compared with that calculated using a treatment planning program.

Methods and materials

Phantom design

A box was made of Perspex (PMMA) with internal dimensions 15 cm × 15 cm × 18 cm. An insert of expanded polystyrene 7.5 cm × 15 cm × 10 cm was fixed in the box at one side, extending from 3 cm to 13 cm below the surface. The box was filled with dosimetric gel to within 1 cm of the surface. The polystyrene was wrapped in clingfilm to prevent seepage of gel. The total volume of gel used was 2.7 l.

Production of Fricke gel

The final concentrations of reagents within each litre of gel were 1 mM ammonium iron (II) sulphate, 1 mM sodium chloride and 25 mM sulphuric acid; all these were AnalaR grade from BDH Chemicals. The concentration of agarose (type 1-A from Sigma Chemical Company) was 1% by weight.

To make 2.75 l of gel, the reagents for the Fricke solution were dissolved in 1.0 l of de-ionized water and oxygenated by passing oxygen through a sintered glass bulb.

The agarose was added to 1.0 l of de-ionized water, stirred for half an hour and heated to 120°C in a pressure cooker. It was cooled to 100°C and diluted to 1.75 l with boiling de-ionized water. This solution was then oxygenated using a sintered glass bulb whilst cooling to 60°C before the Fricke solution was added. The mixture was stirred thoroughly and bubbles removed by suction before the gel was poured into the Perspex mould. The gel was placed in a refrigerator to solidify and left for several hours at room temperature before irradiation.

Irradiation

Cobalt-60 radiation from a TEM MS-80 cobalt unit was used. The field size was 10 cm × 10 cm with a source-surface distance of 80 cm. The dose given corresponded to 45 Gy at a depth of 0.5 cm below the surface of the gel.

Magnetic resonance imaging

A Picker 2055 HP magnetic resonance imager operating at 1.5 Tesla was used to acquire two sets of images immediately after irradiation. An inversion-recovery sequence (repetition time (TR) 2000 ms, inversion time (TI) 600 ms) gave a T_1-weighted image, and a spin-echo sequence (TR 2000 ms, echo time (TE) 30 ms) gave a proton-density weighted image. The parameters for both sequences were: a 25 cm field of view; an acquisition matrix of 256 × 256; a slice thickness of 10 mm and two signal averages. From these two data sets a map of T_1 values was calculated using software provided by the

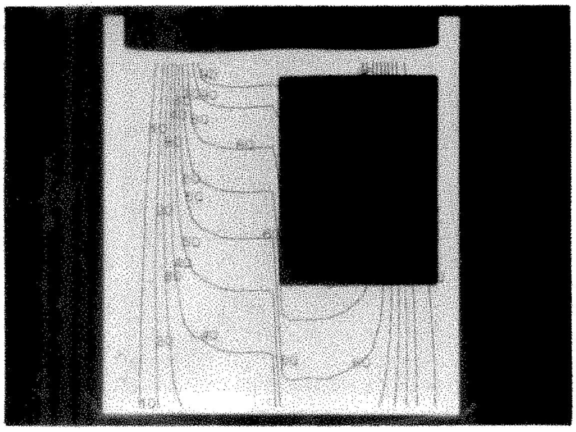


Figure 1. Isodose distribution for 10 cm × 10 cm cobalt beam at 80 cm corrected for inhomogeneity. The isodoses are superimposed on a CT image of the phantom.

manufacturer. Previous work (Wilkinson, 1989) has demonstrated the linear response of this MR system to T_1 by using calibrated gadolinium-doped agarose gels.

Radiotherapy treatment planning

A computed tomography (CT) image was obtained using a Siemens Somatom Plus system and subsequently transferred to an IBM AT compatible computer. The electron densities relative to water of the gel and the expanded polystyrene, as determined from the CT attenuation values, were 1.007 and 0.06, respectively. The expanded polystyrene is of lower density than lung. This was chosen to give a sharper contrast between the two sides of the phantom and to provide a more severe test of a treatment planning algorithm than would be provided by a region of higher density.

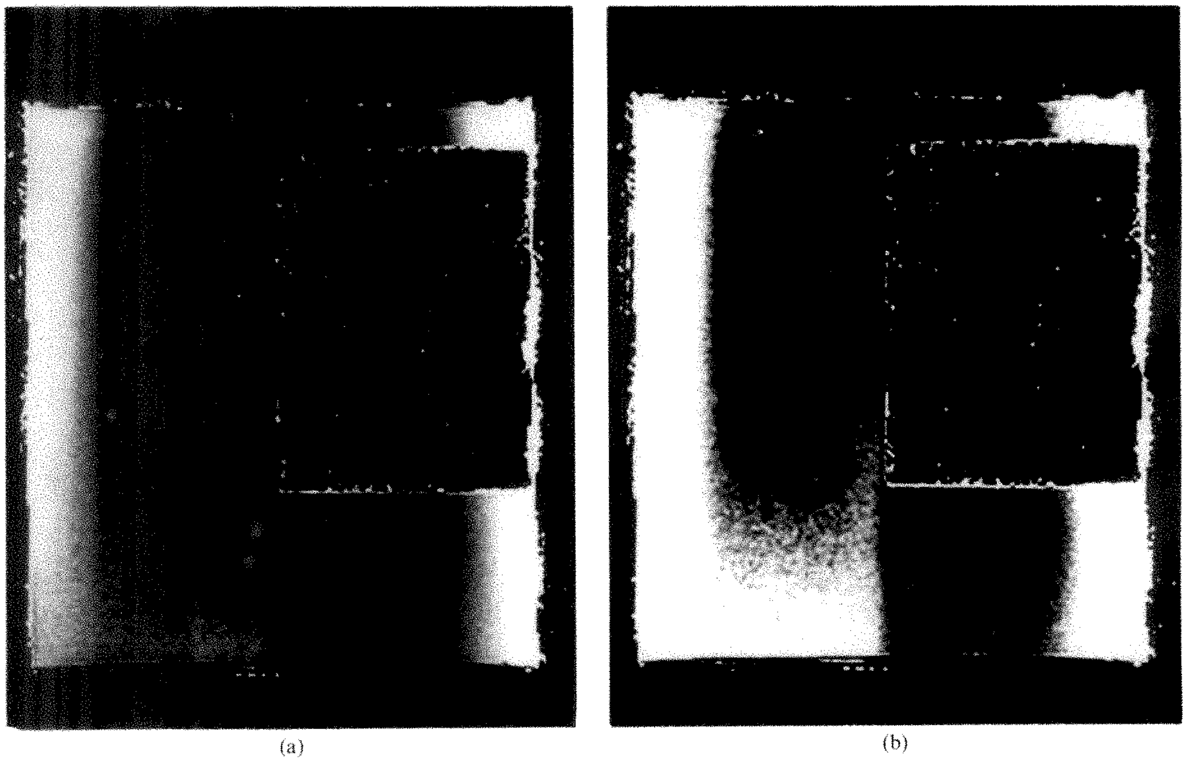
A dose distribution was calculated using a modified Batho power-law algorithm (Thomas, 1991) incorporated into a treatment planning program written in C. This algorithm has been tested, using ionization dosimetry, for a wide range of energies and field sizes.

Results and discussion

The isodoses superimposed on the CT image are shown in Figure 1.

Figures 2 (a & b) show the computed T_1 map, with two different window settings. The reciprocal of T_1 varies linearly with dose, so the darker the image the higher the dose. Visually, there is a close resemblance between this image and the isodose distribution.

Figure 3 shows the MR values of $1/T_1$ plotted against calculated dose at various points in the phantom. The triangles show points measured on a line 2.5 cm from the central axis of the beam (away from the inhomogeneity), the circles show points in the region below the inhomogeneity. These lie slightly to the right of the



(a) (b)

Figure 2. Computed T_1 MR images of the phantom in the same plane as for Figure 1. (a) Shown with a window width of 490 ms, centred on 284 ms and (b) with a window width of 114 ms, centred on 253 ms.

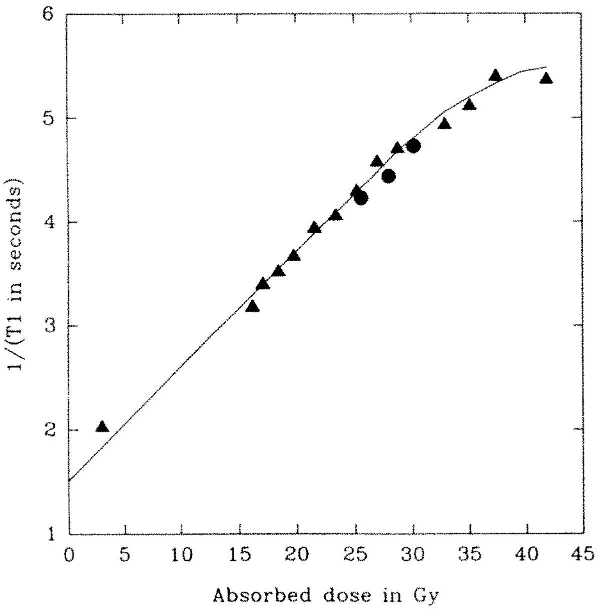


Figure 3. ($1/T_1$) MR values plotted against calculated dose at a number of positions in the phantom. The circles are for points beneath the inhomogeneity and the triangles are for points away from the inhomogeneity.

curve through the triangles, suggesting that the treatment planning algorithm may be overestimating the dose behind the inhomogeneity by a few percent. This overestimate could result from the fact that the 1-dimensional power-law algorithm treats all inhomogeneities as semi-infinite slabs and makes no correction for loss of scatter in more complex situations. Further work will be required to determine whether this shift is real or within experimental error.

The curve through the triangles is linear to approximately 30 Gy and shows signs of saturation at higher doses. This is in agreement with the results of Shultz et al (1990).

Ordinary purity de-ionized water and AnalaR reagents have given satisfactory results. It does not seem to be necessary to use the triple distilled water and ultra-high purity reagents required for conventional Fricke dosimetry.

Acquiring the MR imaging of the phantom as soon as possible after irradiation minimized migration of the Fe^{3+} ions within the gel. As recently discussed by Day (1990), migration of ions is one of several practical aspects of the technique that remain to be evaluated.

Conclusions

Fricke gels show great promise for the visualization of three-dimensional dose distributions in phantoms.

In this paper the feasibility of the method has been demonstrated using a treatment plan with a simple irradiation geometry. The technique readily lends itself to determination of dose distribution in more complex situations, where it is harder for treatment planning programs to make accurate predictions. Examples of such situations include conformational therapy, stereotactic radiosurgery and the calculation of dose near inhomogeneities in electron therapy.

The doses required are of the order of tens of Gy. Although these are higher than those needed for ionization chambers, film or thermoluminescent dosemeter, they should not in general, lead to unacceptably long irradiation times. Doses of the order of tens of Gy are common prescriptions in radiosurgery. Verification of standard treatment plans, or conformational therapy with multi-leaf collimators, will involve gel irradiation times of less than half an hour, since dose-rates at the isocentre of linear accelerators are typically a few Gy per minute.

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Case reports

Magnetic resonance imaging of peritoneal leiomyosarcomatosis

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Diffuse peritoneal and omental metastatic disease is a well recognized phenomenon and usually results from primary gastrointestinal tract or epithelial ovarian tumours. Leiomyosarcoma, an uncommon malignant neoplasm of smooth muscle origin that tends to arise in the genitourinary tract, retroperitoneum, alimentary tract or soft tissues, only infrequently gives rise to peritoneal or omental metastases. We report a patient with a primary high-grade leiomyosarcoma of the uterus, who subsequently developed diffuse peritoneal metastatic disease, demonstrated by magnetic resonance imaging (MRI) and confirmed surgically. These unusual MRI appearances do not appear to have been reported previously.

Case report

A previously well 43-year-old woman presented with polymenorrhagia and was found clinically to have a uterus enlarged to 12–14 weeks' gestational size. She underwent a routine hysterectomy, and at laparotomy an enlarged fibroid uterus (15 cm × 9 cm × 7 cm) was removed and a right haemosalpinx resected. The ovaries were normal and were conserved. Histological examination of the resected uterus showed a high-grade (mitotic count of more than 10/10 high-power field) leiomyosarcoma in a partially necrotic pedunculated fibroid of 5 cm diameter situated within the upper uterine cavity. There were several foci of myometrial invasion, the deepest extending to 0.3 cm from the serosal surface. Some regions of hyalinization and necrosis were present. Islands of tumour abutted but were not invading thin-walled blood vessels. The histology of the right fallopian tube showed chronic salpingitis only.

No additional treatment was given at that time. At follow-up 4 months later she was found to have a large abdominopelvic mass, which was considered to represent either recurrent leiomyosarcoma or possibly a primary ovarian neoplasm. MRI was carried out on a 0.15 T resistive system using sagittal SE 2000/80, sagittal SE 1840/60, axial SE 500/40 and coronal IR 1660/400/40 sequences. This showed the pelvis and lower abdominal cavity to be filled with multiple well defined spherical masses that, in some regions, formed conglomerate masses of up to 10 cm diameter (Fig. 1). There was loss of tissue planes against adjacent structures though no frank invasion was identified. The masses were predominantly of intermediate to low signal intensity on all pulse sequences, similar, though not identical, to that of striated muscle. Some lesions displayed centrally increased signal intensity on T_2-weighted sequences and reduced signal intensity on the IR sequence. There was a small amount of ascitic fluid. No lymph node enlargement was identified.

A further laparotomy was undertaken, which confirmed the abdomen and pelvis to be full of rounded rubbery tumour masses of up to 10 cm diameter. There were numerous large vessels supplying these areas and the omentum was adherent to much of the tumour. A small quantity of ascitic fluid was present. Resection was impossible, but several tumour nodules were excised and histological examination confirmed the presence of leiomyosarcoma of similar morphology to the primary tumour. There was no evidence of ovarian malignancy. Palliative chemotherapy using the CYVADIC regime (cyclophosphamide, vincristine, adriamycin, and DTIC) was commenced.

Discussion

Uterine leiomyosarcoma is a rare malignancy and the diagnosis often remains unsuspected up to the time of histological examination, as exemplified by this case. In uteri excised because of the presence of symptomatic leiomyomas, the incidence of leiomyosarcoma is of the order of 0.7% (Lawler et al, 1990). The prognosis is generally poor (Bartisch et al, 1968) but appears better when there is no macroscopic tumour spread beyond the pseudocapsule of gross vascular invasion (Gudgeon, 1968). Both of these apparently better prognostic features were present in the case discussed.

MRI is an excellent technique for imaging uterine leiomyomas and is capable of accurately demonstrating their number, size, location and the presence and extent of degeneration (Hricak et al, 1986; Kerslake & Worthington, 1990). The prospective diagnosis of sarcomatous degeneration within uterine leiomyomas has not, to our knowledge, been reported and in our experience has not been possible (Kerslake & Worthington, 1990).

In a recent report, dissemination of leiomyosarcoma within the peritoneal cavity was observed in 14 out of 118 patients with tumours arising from a variety of primary sites. Of the 19 patients with a primary uterine leiomyosarcoma, only two had peritoneal metastases (McLeod et al, 1984). Peritoneal spread may occur

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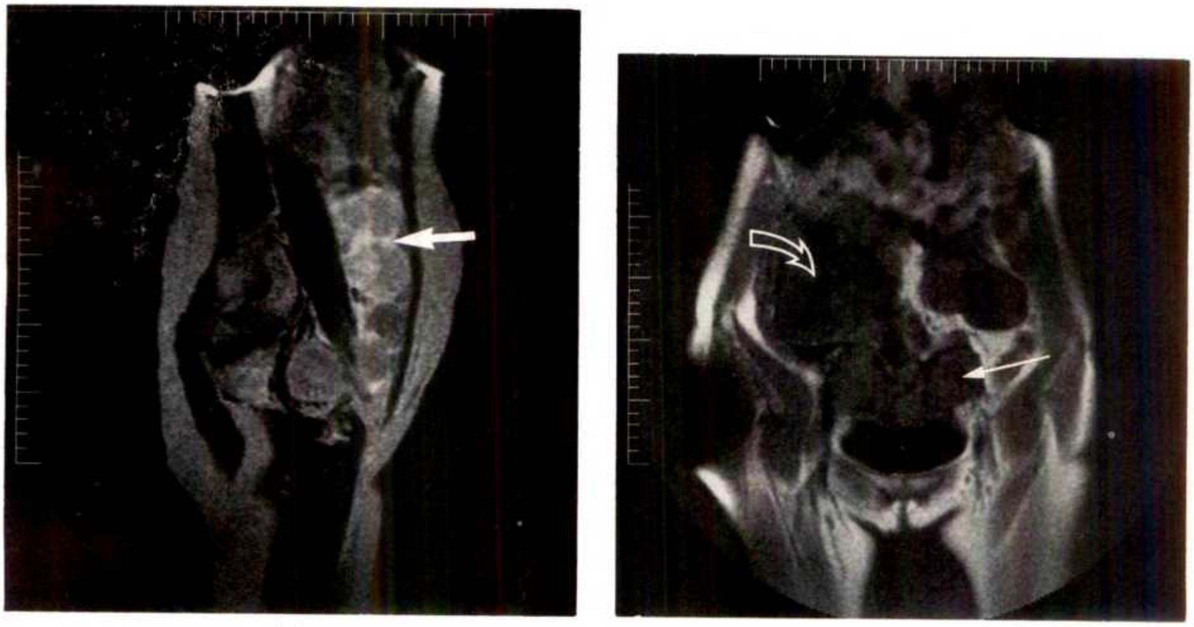
(a) (b)

Figure 1. (a) Parasagittal SE 2000/80 and (b) coronal IR 1660/400 images. Multiple discrete and conglomerate tumour masses (curved open arrow) are present within the pelvis and lower abdominal cavity. They are of intermediate to low signal intensity but some show central hypointensity on the IR sequence (fine arrow). A small volume of ascites is present (bold arrow).

directly through the mesentery, by embolic metastases or by intraperitoneal seeding via ascitic fluid. Computed tomography (CT) has been found useful in the detection of peritoneal and serosal deposits of leiomyosarcoma (McLeod et al, 1984; Choi et al, 1990). The gross morphological appearances on CT of central low-attenuation changes within large soft-tissue masses correlate well with the central necrosis or cyst formation seen on pathological examination of high-grade tumours (Choi et al, 1990).

Ascites has been reported to occur in 50% of patients with peritoneal leiomyosarcomatosis in one series (McLeod et al, 1984) but in none of another (Choi et al, 1990). The presence of multiple peritoneal tumour masses in the absence of ascites is relatively unusual with advanced ovarian or gastrointestinal malignancies and is considered by some authors to favour a diagnosis of either peritoneal leiomyosarcomatosis (Choi et al, 1990) or the apparently benign condition of leiomyomatosis peritonealis disseminata (LPD) (Renigers et al, 1985). There is some debate as to the benign nature of LPD as patients with multiple peritoneal deposits of low-grade leiomyosarcoma may present very similar gross appearances.

The differential diagnosis of multiple peritoneal masses includes metastatic ovarian or gastrointestinal neoplasm, lymphoma, leiomyosarcoma, other sarcomas and LPD. In this particular case, the question of an ovarian malignancy had been raised clinically. Although the ovaries were not positively identified by MRI, the very well defined spherical masses of predominantly low signal intensity would be atypical for either primary or metastic ovarian neoplasm. Primary ovarian carcinoma of predominantly low signal intensity on T_2-weighted images has not been reported (Weinreb et al, 1990). Recurrent or residual ovarian carcinoma is typically of very high signal intensity when heavily T_2-weighted or STIR sequences are employed. Using these sequences, even small-volume recurrences may be detected owing to their conspicuity against a background of suppressed signal from bowel contents and pelvic fat (Kerslake et al, 1990).

The enhanced vascular supply encountered at surgery was not apparent from the MR images, even in retrospect. In all other respects, however, MRI gave an accurate depiction of the gross morphological features that were encountered at operation. The presence of poorly defined central regions of hyperintensity on T_2-weighted images correlated with regions of necrosis and cyst formation shown pathologically, in keeping with a high-grade leiomyosarcoma.

In this case the antecedent history of a primary uterine leiomyosarcoma enabled a specific diagnosis to be suggested following MRI. However, peritoneal leiomyosarcomatosis may occur in the absence of a known primary tumour. Thus, when MRI demonstrates multiple, spherical, well defined peritoneal and mesenteric masses with central heterogeneity and with or without small volumes of ascites, peritoneal leiomyosarcomatosis should be considered amongst the differential diagnosis, even in the absence of a known primary tumour.

Acknowledgments
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The use of ^{123}I-Hippuran renography in the management of synchronous bilateral upper urinary tract transitional cell carcinomata

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Bilateral simultaneously occurring malignant tumours of the upper tracts are very rare, and present the difficult problem of preservation of renal function and adequate tumour clearance. We report such a case and discuss the difficulties and value of the modern methods of management, including ureteroscopy and ^{123}I-Hippuran gamma camera renography with creatinine clearance to assess total and split renal function and recovery.

Case report

A 62-year-old housewife was referred with right loin and back ache associated with haematuria. Two years earlier she had been investigated for right loin pain without haematuria and had normal excretion urography at that time. A repeat urogram revealed a radiolucent filling defect in the upper pole calyx of the right kidney (Fig. 1a), with hydronephrosis and hydroureter on the left side resulting from probable tumour in the distal ureter (Fig. 1b). Serum creatinine was normal. A ^{123}I-Hippuran renogram demonstrated the obstructed left kidney to contribute 36% of global function.

At initial cystoscopic assessment the urethra, bladder and ureteric orifices were normal. Ureteroscopy was not attempted on the left as the developing urographic appearances were considered to be pathognomonic of ureteric tumour (Fig. 1b). Right ureteroscopy (9.5 FG) was successful in reaching the pelvis and tumour-like fronds were seen in the upper pole, but adequate biopsy material could not be obtained. Right retrograde ureteropyelogram appeared to confirm a right pole tumour, although pelvic urine draining from the catheter surprisingly did not subsequently provide positive cytological proof of malignancy.

Following external-beam radiation to the left hemipelvis, the distal left ureter was excised (Fig. 2b), and reimplanted into the bladder using the psoas hitch procedure. Intraoperative frozen section confirmed that the distal end of the remaining ureter was tumour free. A subsequent histological section confirmed a Grade 2 WHO papillary transitional cell carcinoma without evidence of invasion into the ureteric wall.

Following surgery the total glomerular filtration rate (GFR) as measured by creatinine clearance improved to 95 ml/min after 7 days, with split renal function tests showing that the

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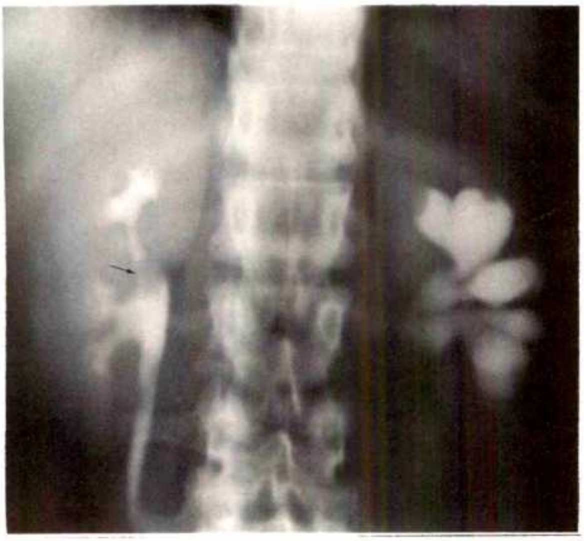
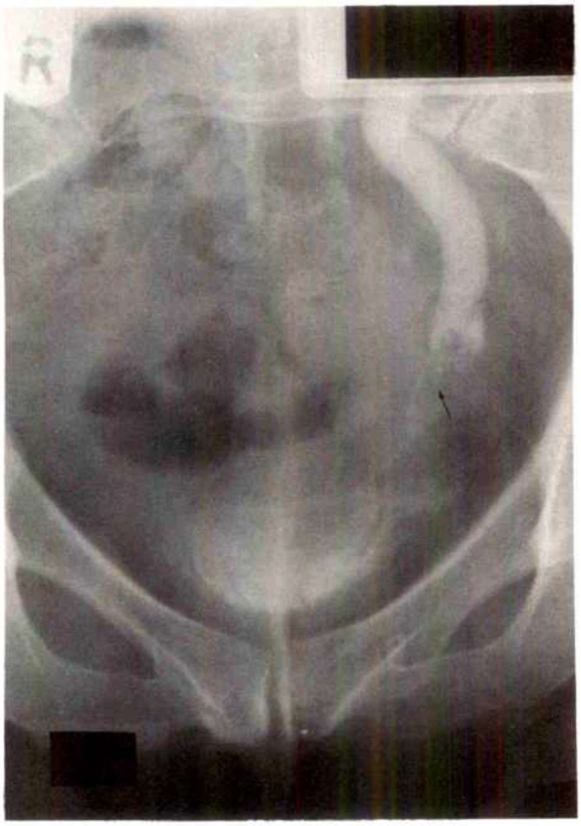


(a)



(b)

Figure 1. (a) View of the upper tracts shows tumour at the right upper pole and left hydronephrosis. Note that the lesion indicated by the probe in Fig. 2a is not visible on the radiograph. (b) Post-micturition radiograph at 3 h showing clear evidence of a left lower ureteric tumour.

right side contributed 73% (69 ml/min) and the now non-obstructed left side 27% (26 ml/min; Fig. 3). This latter figure indicated that after the initial pre-operative renogram significant left-sided deterioration had occurred prior to left ureterectomy, and therefore second stage surgery was delayed in the hope of further recovery of the left kidney. Six weeks later the total GFR was essentially unchanged at 84 ml/min but further ^{123}I-Hippuran renography demonstrated that the left kidney had improved and now contributed 46% to overall renal function (42 ml/min). Serum creatinine was 0.08 mmol/l and was stable; immediately prior to exploration of the right kidney creatinine clearance again improved marginally to 92 ml/min.

At laparotomy there was no extra renal or ureteric spread of tumour. An upper partial nephrectomy to preserve maximal renal function had been considered, but no separate polar vessels were identified and left renal recovery precluded the need for complex surgery. A right radical nephroureterectomy was performed and on opening the specimen (Fig. 2a), a second smaller tumour was seen in the lower part of the pelvis. Subsequent paraffin sections showed multifocal areas of papillary and flat transitional cell carcinomata of WHO Grade 2, both in the renal pelvis and at various points in the ureter, though no evidence of intramural invasion was identified. The post-operative course was uneventful and 6 months following surgery the patient is well with a serum creatinine level of 0.13 mmol/l and GFR of 50 ml/min (Fig. 3).

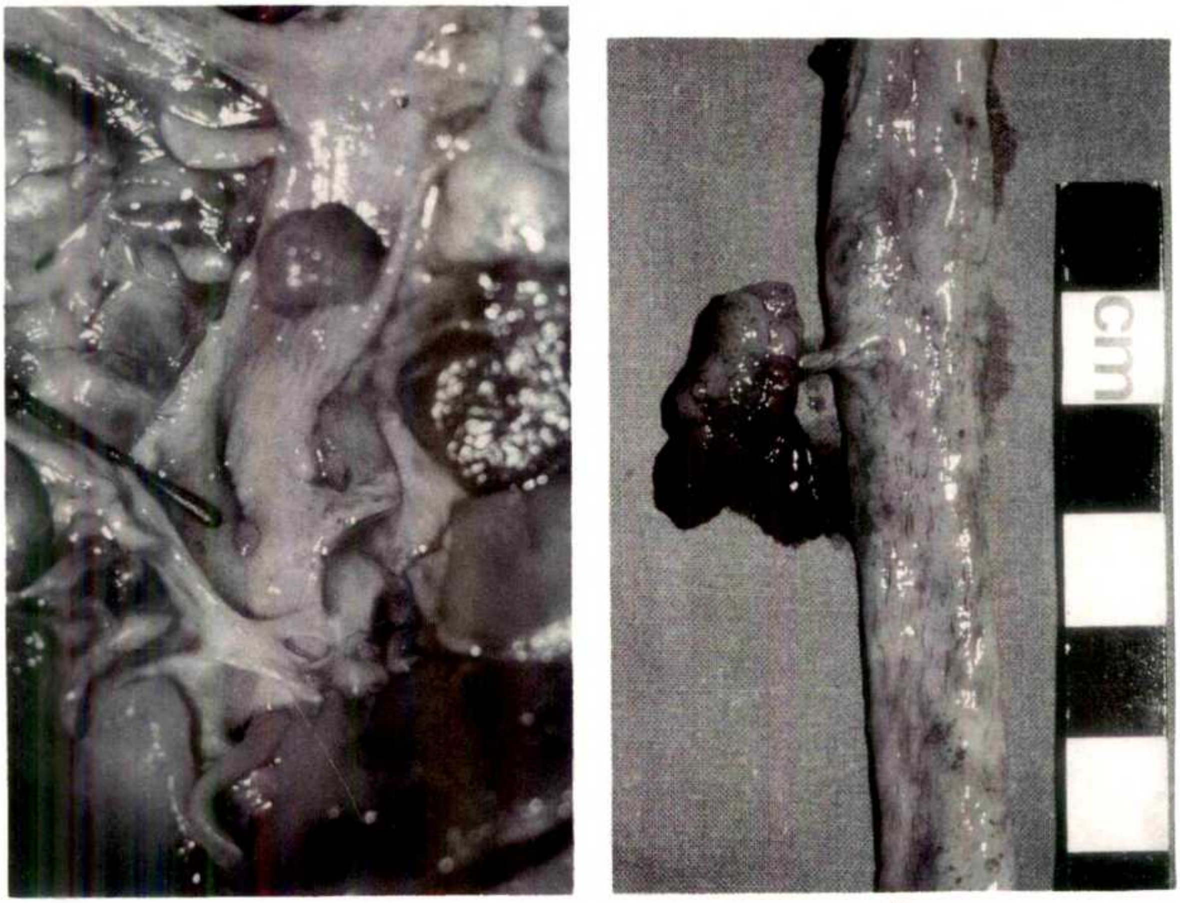
Discussion

Primary ureteric tumours represent 1–2% of all tumours of the upper urinary tract (Werth et al, 1981) and the presentation of synchronous bilateral upper tract tumours is very rare (Daly et al, 1988).

Apart from the well known risks of invasive urothelial cancer affecting the upper tracts, patients with bilateral disease pose difficult questions of management which may in part be answered by the application of modern nephro-radiological and endourological theory and technique.

Recent studies in patients with obstructive uropathy (Jones et al, 1988) show clearly that a period of at least 2 weeks is desirable for the nephron to attain optimum recovery from the obstructed state; furthermore, careful split urine collections with repeated renography and derived percentage function may provide precise information on the progress of each renal unit. In this case such repeated measurements (Fig. 3) enabled a clear surgical decision to be made for radical right nephroureterectomy, a decision favoured by the known incidence of field change (Heney et al, 1981; Werth et al, 1981) and seedling growths in upper tract tumours. This choice was subsequently vindicated by the discovery of disease within the right pelvis and ureter which was not identified either by radiological or ureterscopic techniques (Fig. 2a). Failure of the left kidney to recover to a GFR capable of sustaining life might have dictated an attempt at partial right nephrectomy, possibly including "bench" surgery with organ relocation and ureteric reimplantation.

The risk of further overt tumour arising within the remaining kidney must be high, particularly if the excised ureteric tumour was a seedling from an as yet undetected primary. Ureteroscopy with a rigid or flex-



(a) (b)

Figure 2. (a) High-power view of the right renal pelvis showing a plum-like tumour in the upper pole calyceal neck and a second lesion (indicated by probe) at the mouth of the middle pole calyx. The ureter drains from the pelvis inferiorly. (b) Pedunculated lesion of the left lower ureter with attached blood clot on the inferior margin.

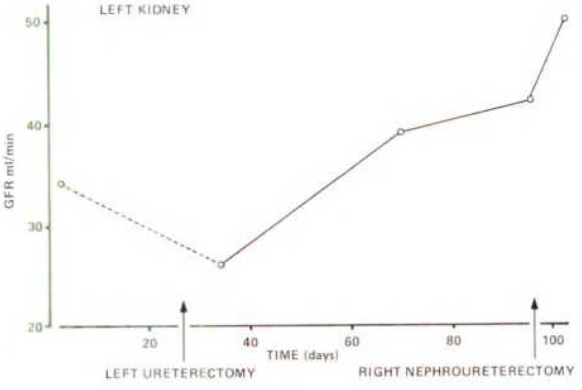


Figure 3. Changes in left kidney GFR as measured by creatinine clearance and gamma camera renography. Deterioration in function clearly occurred (dotted line) in the month preceeding surgery (see text for details).

ible instrument including facilities for biopsy and resection will be important in the further management of this case. To this end, elective refluxing reimplantation in the optimum position for easy instrumental access has facilitated the regular review cystouretero-pyeloscopies that will be required in the future. Furthermore, free reflux —particularly on micturition— into the remaining renal units allows the possibility that intravesical chemotherapeutic agents such as mitomycin C might be employed in the future to control recurrent urothelial disease within both upper and lower urinary tracts.

In summary the management of this case has been assisted by modern theory concerning the recovery of obstructive renal failure and the availability of sophisticated radiological and endourological techniques. Estimation of renal function before nephrectomy enabled a confident prediction of avoidance of renal replacement therapy to be communicated pre-operatively to the patient.

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Magnetic resonance imaging of penile rhabdomyosarcoma

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In recent years the management of sarcomas of the penis has undergone a radical change. The trend of treatment has shifted away from mutilating surgery (Ashley & Edwards, 1957; Pratt & Ross, 1969), which often left the phallus functionally inadequate and the patient a psychological cripple, to one of conservation of the penis, in selected patients. Adjuvant chemotherapy and excision of the tumour with preservation of the penis has been shown to hold promising results in two patients (Pak et al, 1986; Dalkin & Zaontz, 1989). This has been made possible, largely because of improved chemotherapy of sarcomas in general (Hays et al, 1982a & b).

Magnetic resonance (MR) imaging has been reported previously to be of value in the evaluation of penile pathology, such as Peyronie's disease, carcinoma of the urethra and metastases to the penis (Hricak et al, 1980; Hricak et al, 1988). This report illustrates the use of MR imaging in the staging and follow-up of a soft tissue sarcoma of the penis. This is the first reported case of the successful treatment of an infiltrating sarcoma of the penis, by chemotherapy alone. Evaluation of the response to chemotherapy is dependent on accurate and sensitive imaging modalities. MR imaging seems to fill this role admirably.

Case report

A 3-year-old white male presented with a mass, of 4 months duration, on the dorsum of his penis. The child was otherwise asymptomatic. Physical examination revealed a hard mass

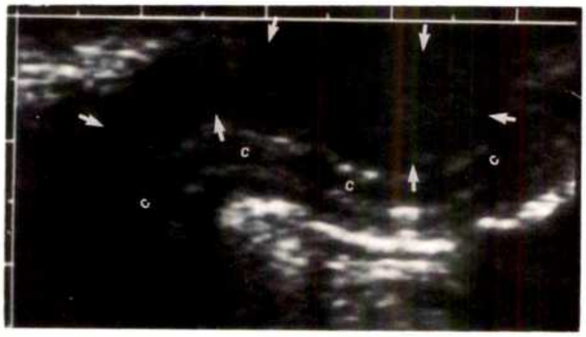


Figure 1. Longitudinal sonogram of the penis, performed with a 5 MHz linear transducer. The mass (arrows) is of uniform echogenicity and is superficial to the corpora cavernosa (C).

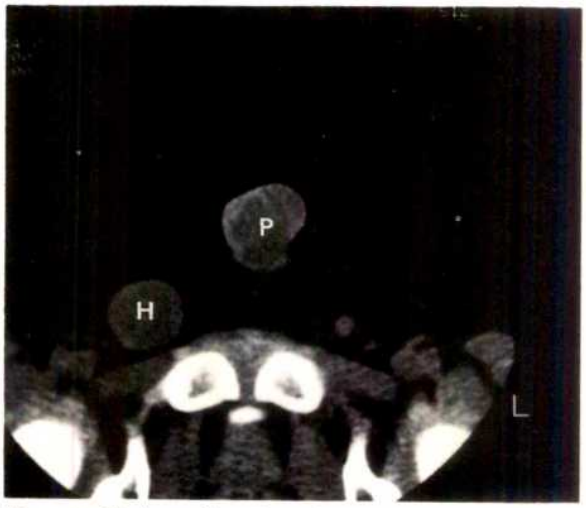
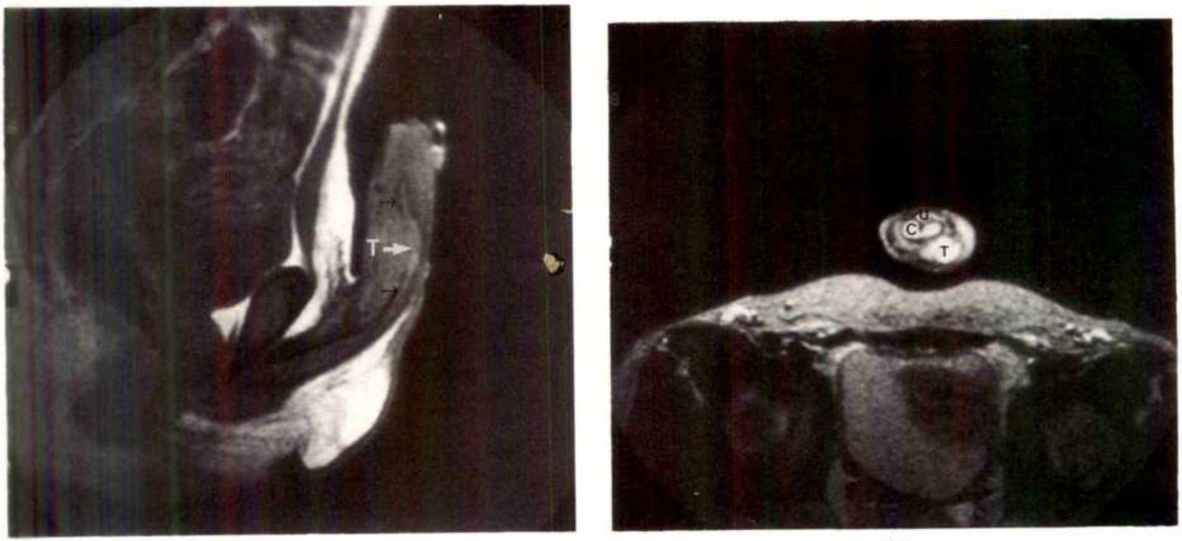
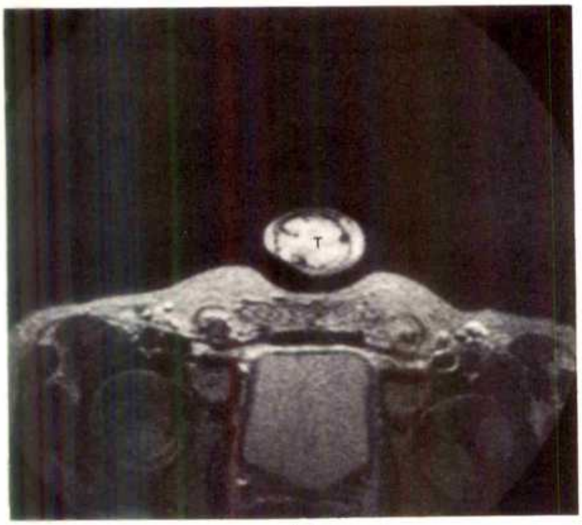


Figure 2. CT shows distortion of the penile contour (P); but fails to delineate both the discrete mass or the corpora. There is a right inguinal hernia (H).



(a) (b)



(c)

Figure 3. MR of the penis: before chemotherapy. (a) Sagittal T_1-weighted image (TR = 633, TE = 26 ms) shows the tumour (T). The normal low signal of the tunica albuginea (black arrows) around the left corpus cavernosum is interrupted by the tumour (white arrow). (b) Axial T_2-weighted image (TR = 2000, TE = 80) shows high signal intensity of the mass (T). The corpora cavernosa (C), corpus spongiosum and urethra (U) are clearly demonstrated. (c) A more proximal image (TR = 2000, TE = 80) shows infiltration of the corpora cavernosa by the tumour (T).

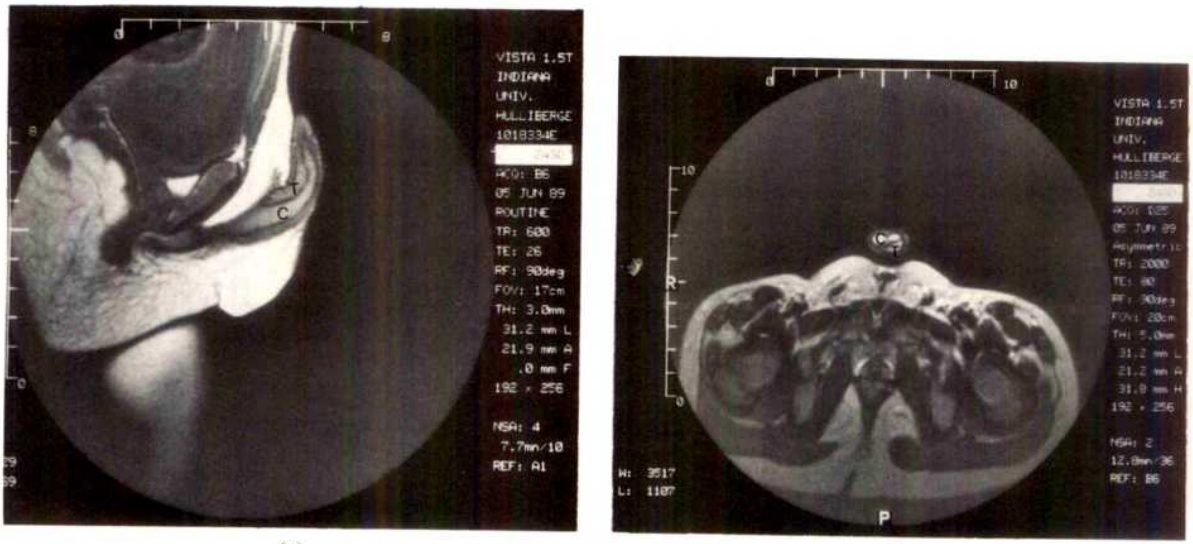
extending from the corona to the base and circumscribing the penis. High resolution penile ultrasonography was performed with a computed sonography unit (Acuson 128; Acuson, Mountain View, CA, USA) using a 5 MHz linear transducer. Ultrasonography revealed the mass to be solid and superficial to the corpora cavernosa (Fig. 1). Computed tomography (CT) (GE 9800, General Electric Medical Systems, Milwaukee, WI, USA) was performed with the penis taped to the anterior abdominal wall. Slices of 5 mm thickness were obtained which showed distortion of the penile contour, but failed to delineate a discrete mass from the corpora (Fig. 2). MR imaging was performed with a 1.5 Tesla super-conducting magnet (Picker International, Cleveland, OH, USA). Spin echo images were obtained in axial and sagittal planes, with a slice thickness of 5 mm. MR was able to differentiate the tumour from the corpora and demonstrated infiltration of the corpora cavernosa (Fig. 3c).

The mass was confirmed to involve the corpora on surgical exploration of the penis. Removal of the mass with negative margins was not possible without mutilating the penis. Several biopsies of the mass were taken and on pathological examination were reported as undifferentiated sarcoma.

After a negative metastatic workup, the patient was started on a multiagent chemotherapy programme, which included vincristine, adriamycin, cyclosphosphamide, cisplatin and dactinomycin. The response to treatment was monitored with MR imaging of the penile mass. At 20 weeks follow-up, the mass had decreased in size and the tunica albuginea was intact (Fig. 4a). Re-exploration with removal of the non-encapsulated residual mass was performed at this time. Pathological examination revealed no viable tumour. Chemotherapy is to continue for a total of 104 weeks, in accordance with the protocol.

Discussion

Several imaging modalities, including cavernosography (Raghavaiah, 1978; Escribano et al, 1987),



(a) (b)

Figure 4. MR of the penis: after chemotherapy. (a) Sagittal T_1-weighted image (TR = 600, TE = 26) shows decrease in size of mass (T) and intact corpora cavernosa (C). (b) Axial T_2-weighted image (TR = 2000, TE = 80) shows decreased size of the mass (T) relative to the corpora (C).

urethrography (Hertz, 1990), angiography (Bookstein, 1990), ultrasound (Rosenfeld et al, 1990), CT (Kazam et al, 1990) and MR imaging (Hricak et al, 1980; Hricak et al, 1988) have been applied to penile pathology. Angiography and cavernosography are invasive and hence their use is limited, especially if frequent examinations are required in the follow-up of tumour patients. Urethrography provides only indirect evaluation of penile masses and does not provide information about the extent of the tumour.

High resolution ultrasonography has been used to image the penis in demonstrating strictures (Gluck et al, 1988). Peyronie's plaques have been identified and followed during therapy (Gelband et al, 1981). It has also been used in penile trauma to determine the integrity of the corpora (Dierks & Hawkins, 1983). Ultrasound, however, is operator dependent and studies are difficult to reproduce. Although the pendulous portion of the penis is easily accessible to ultrasonic examination, the more proximal portions of the corpora are difficult to examine because of interference of the pubic bones. In this patient, the mass was determined to be solid (uniform echogenicity) and superficial to the corpora cavernosa (Fig. 1). However, ultrasound did not indicate the extent of infiltration.

In this patient CT was limited to the axial plane and lacked sufficient tissue contrast to separate the tumour from the normal penile structures (Fig. 2).

MR imaging overcomes many of the disadvantages of the other imaging modalities. It is able to obtain images in multiple planes without repositioning the patient and has excellent soft tissue contrast resolution. This is particularly true of the penis where the proximal corpora require multiple imaging planes for complete evaluation. The mass had high signal intensity on T_2-weighted images (Fig. 3b). Determining the relationship of the tumour to the corpora was facilitated by the inherent soft tissue contrast between the mass and the tunica albuginea, which has a high collagen content resulting in a low MR signal (Fig. 3a). Loss of the normal low signal from a portion of the tunica suggested invasion of the corpora (Fig. 3c). This was confirmed at initial surgery.

Following chemotherapy, repeat MR imaging showed the mass to be much smaller and there was no interruption of the low signal intensity from the tunica albuginea, seen in the earlier study (Fig. 4b). A change in the size of the mass denoted a response to chemotherapy. These findings were confirmed on re-exploration and excision of the residual mass, which revealed no viable tumour on pathological examination.

This case report illustrates the superiority of MR imaging to ultrasonography and CT scanning in staging soft tissue tumours of the penis. It is also extremely valuable in determining the response to therapy. At present, MR imaging can neither differentiate between a malignant and benign neoplasm, nor distinguish viable from non-viable tumour. However, used with other clinical and pathological criteria, it proved invaluable in the management of this case of penile sarcoma.

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An unusual presentation of pulmonary alveolar microlithiasis and diaphyseal aclasia

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Keywords: Pulmonary alveolar microlithiasis, Diaphyseal aclasia

Pulmonary alveolar microlithiasis is a rare disease characterized by deposition of calcified bodies in the alveoli, which produce dense sand-like micronodules throughout the lungs. The radiological, pathological and clinical features have been previously well described (Sosman et al, 1957; Thurairajasingam et al, 1975; Prakash et al, 1983; Fraser et al, 1991).

Diaphyseal aclasia (Solomon, 1963; Murray et al, 1990) is one of the more common anomalies of skeletal development with an estimated prevalence of nine per million (Voutsinas & Wynne-Davis, 1983). Inherited as an autosomal dominant trait, most cases present during childhood development owing to deformity and complications; however, milder cases may only be detected later in life by chance.

Both pulmonary alveolar microlithiasis and diaphyseal aclasia demonstrate a familial tendency and have specific radiological features, but they are not known to be related. We present a case of pulmonary alveolar microlithiasis found incidentally while under investigation of skeletal deformity.

Case report

In 1967, a 5-year-old boy was referred to an orthopaedic clinic with right upper limb deformity. His developmental milestones were slightly retarded, but he was otherwise well.

A radiograph of his right humerus revealed an osteochondroma in the upper shaft and an abnormal adjacent lung field. A chest radiograph (Fig. 1) showed a diffuse dense interstitial process with a predominantly nodular pattern. There was

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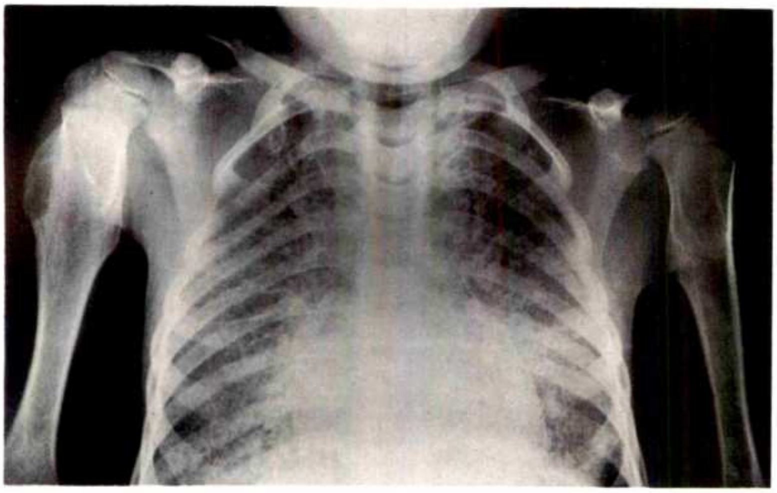


Figure 1. Chest radiograph showing a diffuse dense micronodular process in both lungs, which becomes more confluent centrally where there is slight blurring of the mediastinal borders. Note the osteochondromas in both upper humeri.

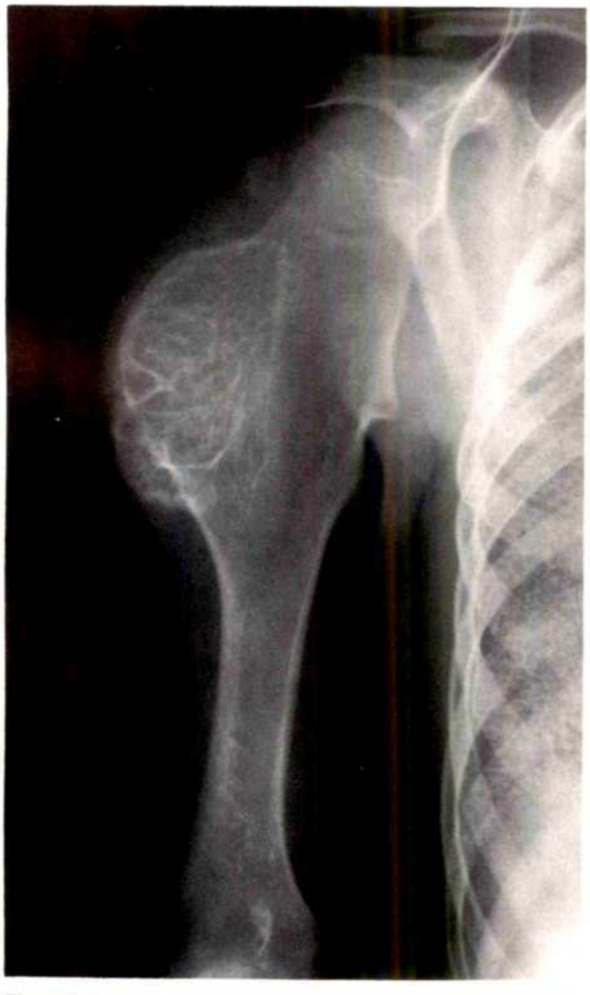


Figure 2. Radiograph of right humerus showing the osteochondroma has increased in size over 3 years. Note the tiny dense punctate nodules in the adjacent lung and negative pleural shadow.

blurring of the mediastinal borders and a faint negative pleural shadow. Further osteochondromas were demonstrated in other parts of the skeleton in keeping with diaphyseal aclasia.

Although the patient was well and had no respiratory symptoms, an open lung biopsy was performed. Histology showed alveoli filled with concentrically laminated smooth calcispherites without fibrosis, appearances diagnostic of pulmonary alveolar microlithiasis.

Over the next 3 years, the osteochondroma of his right humerus enlarged in size (Fig. 2) and was therefore resected. Histologically, the osteochondroma showed no evidence of sarcomatous change. In 1988 (aged 26 years), he presented with a spontaneous left pneumothorax (Fig. 3), which was aspirated successfully and since then he has remained well.

Lung function has been assessed on several occasions since 1987 (Table I) and the trend could suggest a restrictive impairment of ventilation.

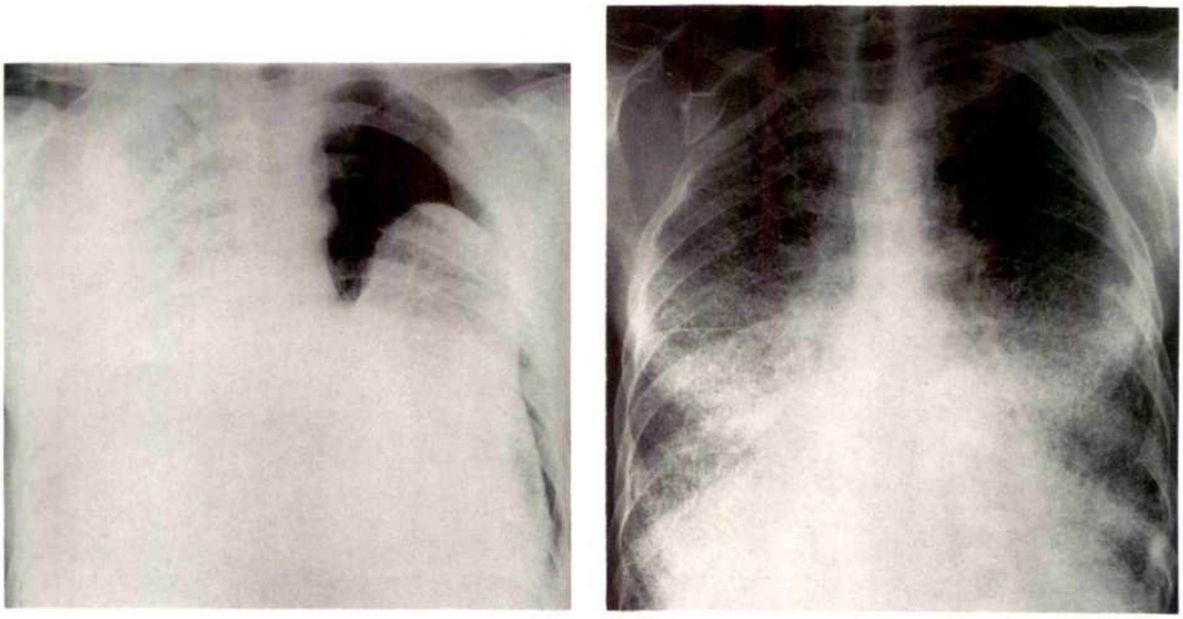
Radiographic examination revealed no evidence of either disease in his immediate family (parents and sister), his maternal relatives (four step-siblings, aunt and uncle) or his paternal relatives (aunt and two siblings).

Discussion

Pulmonary alveolar microlithiasis is a rare disease described in all age groups, from premature still-born twins (Caffrey & Altman, 1965) to an 80-year-old woman (Sears et al, 1971), with a mean age at presentation of approximately 35 years (Thurairajasingam et al, 1975). To date, there are less than 200 reported cases in the literature (Fraser et al, 1991). Although its aetiology remains unknown, approximately half the recorded cases are familial, implicating an inborn error of metabolism. However, this has not been proven. X-ray energy spectroscopy and microscopic infrared spectroscopy have been used to define the nature of the microliths thus helping to explain the pathogenesis of the disorder (Barnard et al, 1987).

The disease is not confined to the alveoli since calcispherites have also been demonstrated in the bronchial walls (Sears et al, 1971), lumbar sympathetic chain and possibly testis (Coetzee, 1970).

Typically the disease is discovered incidentally, making its course difficult to predict. Several cases



(a) (b)

Figure 3. Chest radiographs (a) before and (b) after aspiration of left pneumothorax. Progression of the disease is shown with marked confluence at the bases and almost complete obliteration of the mediastinal and diaphragmatic contours. Note further osteochondromas of both scapulae with consequent deformity of the adjacent ribs.

(Fraser et al, 1991), including our own, have remained asymptomatic for over 20 years; however the disease is usually progressive with development of interstitial fibrosis leading to cyanosis, polycythaemia and eventually respiratory failure with cor pulmonale. Spontaneous pneumothorax, clubbing and haemoptysis have all been reported (Sosman et al, 1957).

Lung function tests are often normal despite the presence of gross radiological abnormality (Sosman et al, 1957); however, a restrictive impairment of ventilation may develop, together with an increase in the alveolar-arterial oxygen gradient and a fall in transfer factor (Prakash et al, 1983).

The pattern of microcalcification is virtually unique and in established cases, with typical radiological appearances and family history, open biopsy is hardly justifiable. Corticosteroids, chelating agents and bronchial lavage have been used to treat the condition with no apparent success (Thurairajasingam et al, 1975; Palombini et al, 1981; Chalmers et al, 1986).

Table I. Lung function tests

Test	Percentage of predicted (mean) normal value	
	January 1987	June 1988
FEV_1	81	85
FVC	79	76
D_LCO	89	68

FEV_1 = forced expiratory volume (litres) in 1 s; FVC = forced vital capacity (litres); D_LCO = diffusing capacity of the lung for carbon monoxide (mmol/min/kPa).

In diaphyseal aclasia (Solomon, 1963; Murray et al, 1991), disordered growth in endochondral bone results in the formation of multiple osteochondromas, typically in the pelvis, shoulder and long bones.

Radiologically the osteochondroma forms a well defined eccentric protrusion continuous with the cortical and trabecular components of the parent bone and has a cartilage-capped apex. The osteochondroma migrates up the shaft of the bone as the physis grows away from it until there is fusion of the adjacent epiphyseal plate when growth of the lesion ceases.

Osteochondromas are often asymptomatic but can produce pressure effects on tendons, nerves and vessels. More importantly, large sessile lesions may interfere with the epiphyseal plate causing disordered growth with resultant bowing, limb-length discrepancy and joint dysfunction.

Sarcomatous degeneration may occur in a stable lesion with a frequency reported as high as 10% by some authors (Solomon, 1963), however it is likely that the true figure is lower, between 1 and 2%, as many cases go unidentified (Voutsinas & Wynne-Davis, 1983).

We have described the clinical and radiological findings in an interesting patient with pulmonary alveolar microlithiasis and diaphyseal aclasia, respectively. The low prevalence of the latter and the rarity of the former make the chances of both diseases occurring in the same patient extremely remote. We do not know of any causative link associating them and it is likely that in the case reported here both diseases occurred spontaneously as new mutations.

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Carcinoma of the ovary: a diagnostic hitch

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Keywords: Ovary, Carcinoma, Transposition

Ovarian transposition during hysterectomy for carcinoma of the cervix is occasionally practised. Transposed ovaries can be variable in position and cause diagnostic difficulty on computed tomography (CT) when operative detail is incomplete (Reed et al, 1989). We report a case of a cystic adenocarcinoma that arose in a transposed ovary and presented as an epigastric mass. We review the literature concerning ovarian conservation with relevance to diagnostic imaging.

Case report

A 36-year-old female patient undergoing a cone biopsy of the cervix was found to have an incompletely excised carcinoma *in situ*. She refused radiotherapy and in January 1984 underwent a modified Werthein's hysterectomy with ovarian conservation. She remained well until December 1989 when she presented with a large epigastric mass. Abdomino-pelvic CT showed a large, well encapsulated cystic mass with a small solid component extending from the epigastrium to the false pelvis (Figs 1, 2) and causing a right hydronephrosis. No information regarding the ovarian conservation was available at the time of scanning but it was suspected that the mass was ovarian in origin given its size and general appearance, despite its atypical

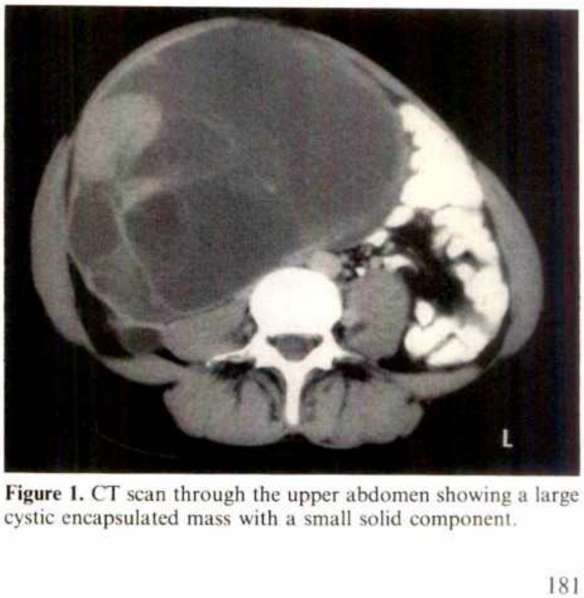

Figure 1. CT scan through the upper abdomen showing a large cystic encapsulated mass with a small solid component.

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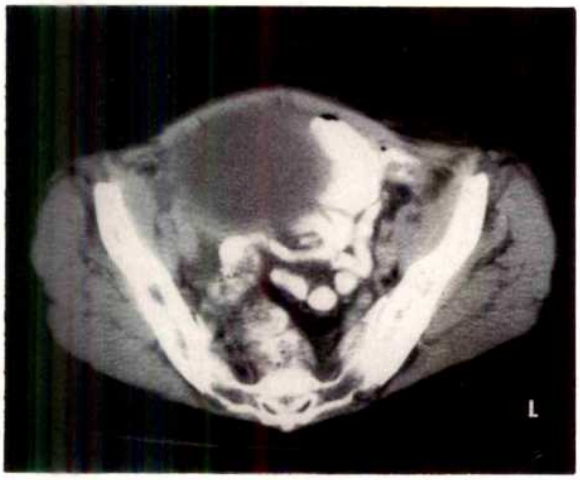

Figure 2. CT scan through the false pelvis showing the origin of the cystic mass.

location. At surgery a large cystic tumour, histologically confirmed to be a moderately well differentiated cystadenocarcinoma, was excised. A normal left ovary was also identified in the false pelvis and there was no evidence of metastatic disease. The patient remains well 15 months later.

Discussion

Ovarian transposition is occasionally undertaken in young patients undergoing hysterectomy for carcinoma of the cervix (Webb, 1975; Hodel et al, 1982; Reed et al, 1989). Ovarian transposition conserves ovarian function and protects the ovaries from any subsequent pelvic irradiation while permitting radical dissection of the parametria and pelvic lymph nodes.

Reed et al (1989) emphasized the diagnostic difficulties posed by transposed ovaries in the absence of adequate operative information. In their cases the transposed ovaries were all sited in the false pelvis sutured to the peritoneum anterior to the ilio psoas muscle and simulated enlarged nodal masses. Other potential sites of ovarian transposition are lateral to the ascending colon, while Leporrier et al (1987) have carried out heterotopic transplantation of an ovary into a subcutaneous compartment in the arm.

In Webb's series (1975) of 64 patients who had ovarian conservation and were followed up for 1–23 years, five subsequently had bilateral oophorectomy for benign disease. Although none of their patients developed ovarian carcinoma, ovarian transposition does create problems as the ovaries cannot be palpated by pelvic examination and monitoring the patient for ovarian pathology becomes more difficult.

In patients who have had a hysterectomy, consideration should be given to the possible ovarian origin of any soft-tissue mass at the above sites. Tumours arising from transposed ovaries have not been reported but are not unexpected. The appearance of any large cystic mass, even in an atypical site, should include ovarian neoplasia.

Acknowledgments

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Case of the month

Now you see it . . . now you don't

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A 52-year-old female presented with a 6 month history of left iliac fossa pain and alteration of bowel habit. She was rather overweight but examination was otherwise unremarkable. A blood count revealed that she was anaemic with a haemoglobin level of 10.1 g dl^{-1}. A barium enema was requested.

Two strictures in the mid-transverse colon were demonstrated (Figs 1 & 2). These appearances were unchanged by intravenous administration of Buscopan 20 mg (hyoscine butylbromide). What is your differential diagnosis?

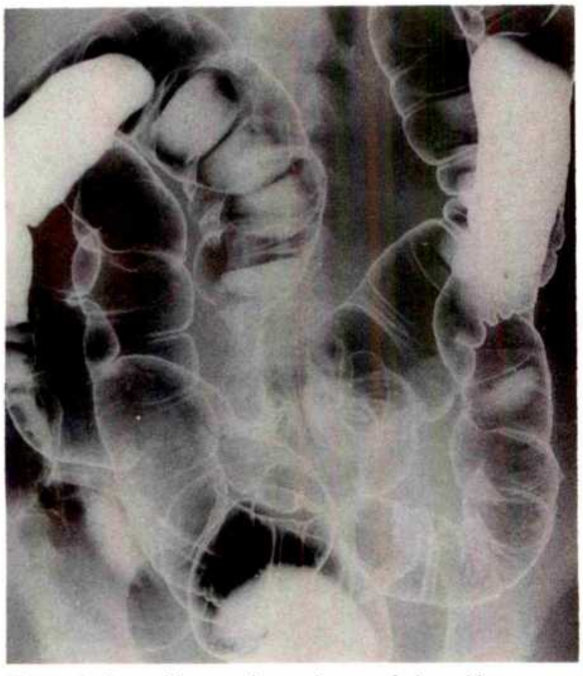

Figure 1. Smoothly tapering stricture of the mid-transverse colon.

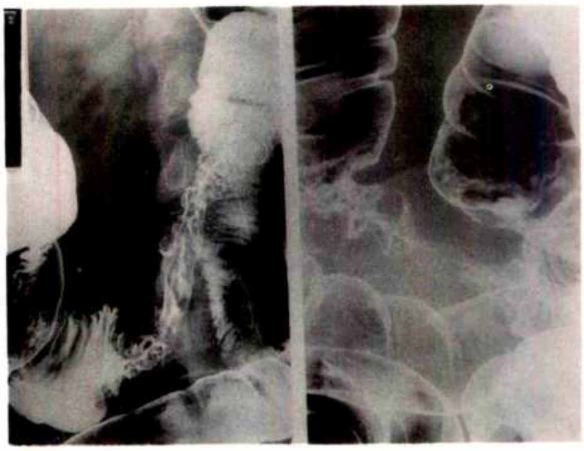

Figure 2. Spot views of this area showing two separate strictures with an area of normal bowel in between. Normal retrograde filling of the small bowel has occurred accounting for opacification of the loop overlying the spine.

Keywords: Barium enema, Colon, Stricture, Ventral hernia

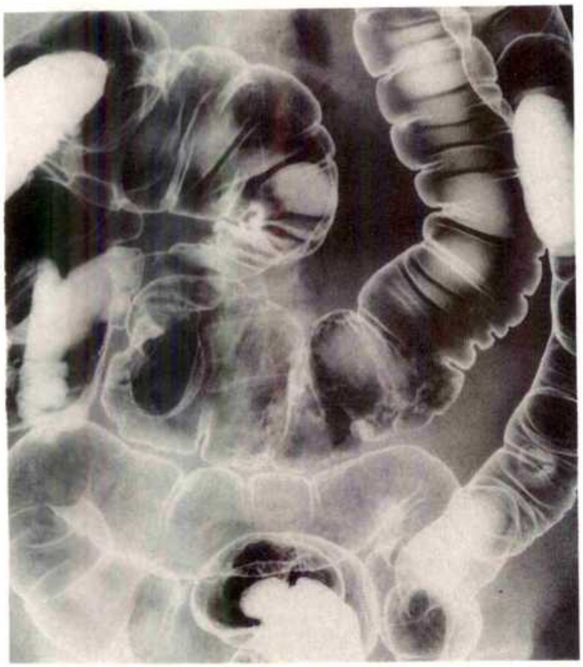

Figure 3. Film taken immediately after reduction of the patient's para-umbilical hernia. Allowing for the presence of some faecal residue and a twist in the proximal transverse colon one can see that the bowel is normally distended with a normal mucosal pattern.

Discussion

These are long strictures affecting adjacent segments of an area of distorted bowel with an abrupt cut-off between normal and abnormal bowel. In some views there appears to be shouldering (Fig. 2). The lumen is circumferentially narrowed and there is a normally distended segment of bowel between the strictures.

Primary colonic neoplasm can invade an adjacent segment of bowel and produce this appearance, as can Crohn's disease. However, there was no evidence of mucosal destruction. Serosal or intramural metastases and endometriosis can produce similar patterns to this, but it would be unusual for them to involve such long segments. The very rare linitis plastica type of primary colonic neoplasm can result in long segment stricturing with relative preservation of the mucosal pattern (Thomas, 1987).

Local segmental spasm could produce these appearances (Thomas, 1987), but judging by the remainder of the large bowel the Buscopan had been effective. Diverticular strictures can affect long segments of bowel with mucosal preservation. Although there are a few scattered diverticula there are none in the region of the stricture; this would be a very unusual site. Local spread from an adjacent primary tumour, primary, or secondary lymphoma would be associated with an extracolonic mass and destruction of mucosa.

A number of benign extrinsic processes can cause colonic strictures. These include pancreatic pseudocysts, colonic retroposition, congenital bands and adhesions (Overton et al, 1954). There was no history of previous surgery in our patient but this is not essential for the formation of adhesions. Inflammation of omentum or the appendices epiploicae, which are particularly abundant in the transverse colon, are well recognized causes (Kyaw & Koehler, 1972).

The possibility of a hernia should always be considered when faced with an atypical colonic stricture. The diagnosis is usually obvious in the case of inguinal, femoral or diaphragmatic hernia. In situations where there is no external mass there may be diagnostic confusion as in the case of obturator hernia and sometimes in Spigelian hernias (Balthazar & Subramanyam, 1983). Similarly ventral hernias such as the para-umbilical variety which rarely contain colon may be easily overlooked.

During air insufflation in this patient the abdomen became noticeably protuberant. On palpation an easily reducible para-umbilical hernia was found to be the cause. The aetiology of a midline "loop-type" stricture of the transverse colon in this patient was therefore obvious. The diagnosis was confirmed by a radiograph taken immediately after reduction of the hernia (Fig. 3).

Considering the prevalence of ventral hernia in the adult population this complication is surprisingly rare. There is only one other report in the recent literature (Forrest & Stanley, 1978) which describes five cases. This is probably because the colon rarely enters the smaller defects while the larger ventral hernias cause little constriction of the bowel contained within them.

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Short communication

An association between leakage of contrast seen on T-tube cholangiogram and subsequent biliary peritonitis

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Keywords: Biliary peritonitis, Cholecystectomy, Cholangiogram

Intraperitoneal leakage of bile can occur after routine cholecystectomy, following removal of the T-tube and following invasive diagnostic procedures, such as percutaneous transhepatic cholangiography and liver biopsy (Corbett et al, 1986; Lygidakis, 1986; Anderson et al, 1988). Spontaneous rupture of the common bile duct causing biliary peritonitis has been described (Kyzer et al, 1986). Bile is a cause of chemical peritonitis. Bacterial contamination of bile leads quite frequently to virulent septic peritonitis (McLaughlin, 1942; Schwartz, 1979). In a recent prospective study of the complications of T-tube drainage after choledochotomy and common bile duct drainage, three cases of biliary peritonitis occurred after removal of latex-rubber tubes in 36 patients (Gillett et al, 1985). PVC tubes, introduced in the 1960s, were known to cause an increased incidence of bile peritonitis (Anderson et al, 1988) after their removal, but it is now standard practice to use latex-rubber tubes.

Methods

The case summaries of four patients who developed biliary peritonitis are presented. In addition, we have assessed the T-tube cholangiograms in a consecutive series of 56 patients and have recorded the outcome after removal of the T-tube. In all these cases latex-rubber tubes sized 12–18 F were used. All patients had a T-tube cholangiogram done at 7–10 days postoperatively. All 56 T-tube cholangiograms were assessed by a consultant radiologist and a surgical registrar who did not know whether the patient had developed a complication when the T-tube was removed. Particular attention was paid to leakage of contrast medium around the T-tube (Fig. 1). The T-tube cholangiogram was performed by slow injection through a 21 gauge butterfly needle that was inserted into the stem of the T-tube. The notes of these patients were subsequently scrutinized for evidence of biliary leak or ascites.

The data were analysed by χ^2-test and the significance taken as $p < 0.05$.

Results

A history of severe abdominal pain after removal of the T-tube and subsequent drainage of frank bile from the peritoneal cavity was a feature of each case (Table I).

A review of the consecutive series of 56 cholangiograms revealed a leak rate of 50%. Clinically obvious biliary peritonitis only occurred in those with a leak at the time of the cholangiogram (Table II).

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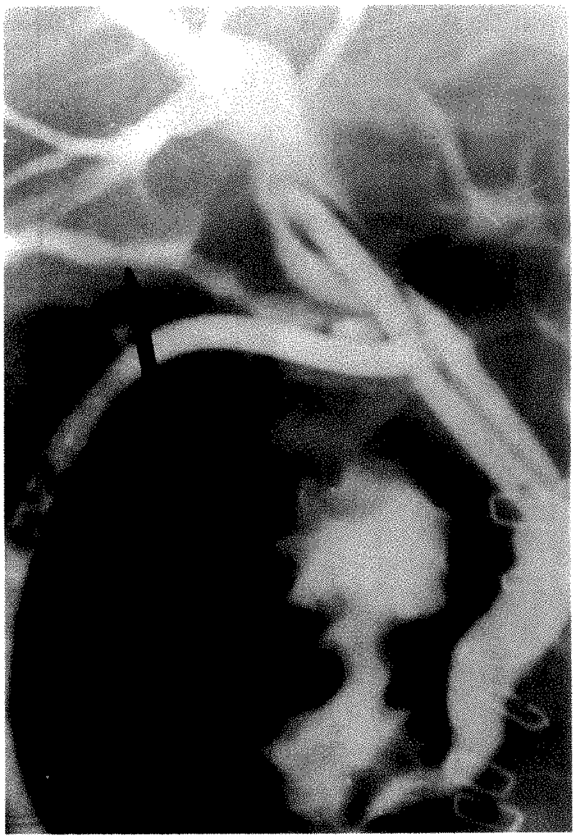

Figure 1. T-tube cholangiogram showing a leak of contrast medium (arrowed).

Discussion

A mild to moderate amount of bile leakage into the peritoneal cavity occurs after routine cholecystectomy, liver biopsy and percutaneous cholangiography. The presence of bile in the peritoneal cavity causes a chemical peritonitis which may resolve spontaneously. However, bacterial infection of the bile can cause septic peritonitis. The incidence of clinical bile leak after removal of a T-tube varies between 7–18% (Gillett et al, 1985; Neoptolemos et al, 1987). We believe that during T-tube cholangiography, attention should be paid not only to the

Table I. Clinical features of four patients who developed biliary leak after removal of the T-tube cholangiogram

	Case 1	Case 2	Case 3	Case 4
Age	23	66	68	61
Sex	F	F	M	F
Operation	Cholecystectomy and choledochotomy	Cholecystectomy and choledochotomy	Cholecystectomy and choledochotomy	Cholecystectomy and choledochotomy
Clinical course after removal of T-tube	Severe abdominal pain. Large right subphenic abscess drained with drainage of 1 l bile under ultrasound guidance	Immediate severe abdominal pain. Laparotomy and drainage of 1 l bile	Re-admitted after 5 days with generalized abdominal pain. 3 l bile drained under ultrasound guidance	Re-admitted after 2 weeks with generalized abdominal pain. 8½ l bile drained by peritoneal tap laparotomy and drainage of intra-abdominal abscess
In-patient stay after diagnosis of leak	10 days	7 days	14 days	28 days

Table II. Incidence of leakage around a T-tube during post-operative cholangiography and subsequent development of biliary peritonitis

	Radiological leak		Total patients
	No leak	Leak	
	28	28	56
Biliary peritonitis	0	4[a]	4

[a] Incidence of leak was significant $p < 0.05$.

presence or absence of retained stones and free flow of contrast into the duodenum, but also to the presence or absence of a leak of contrast medium around the T-tube. In our study 11% of patients with leakage of contrast medium (four of the 28 patients) had clinically significant bile leakage after removal of the T-tube, while none of the patients with no leakage of contrast medium had this complication. If a leak is found on the T-tube cholangiogram, it is now our practice that the T-tube is left in place for another 7–10 days and a cholangiogram then repeated. This would appear to give sufficient time for a track to form around the T-tube preventing spillage of bile into the peritoneal cavity. We have not seen biliary peritonitis of this nature since we adopted this policy.

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Correspondence

(The Editors do not hold themselves responsible for opinions expressed by correspondents)

Computer-based teaching file

THE EDITOR—SIR,

Many radiologists take great pride in their collections of interesting cases, which are invaluable in teaching institutions. At times, either for statistical or research demands, it is necessary to have data at hand in a quick and easy way. The computer is ideally suited to accomplish these functions. However, most commercially available programs contain features which appear unnecessary. Furthermore, more often than not, they require a depth of computer knowledge unfamiliar to most radiologists. A radiologist seldom has the time and the patience to learn all the nuances and intricacies hidden in a program. In addition, lack of experience tends to overload data collection. A third impropriety is that of starting a new venture without adequate personnel support.

In order to overcome these shortcomings we have conceived a program to be used as an intuitive tool for searching and retrieving diagnosis. The undertaking started off with the idea of creating something simple and straightforward. Data should have been few and essential, searching intuitive and fast. Tested with several computer-inexperienced physicians, it was readily understood after a few basic instructions. Intended for radiological use, it was readily extendible to any specialty where diagnosis was required. The fact that only a few essential data are required is an advantage. One interesting facet is the possibility of looking up diagnoses with and/or features (Fig. 1). This permits filtering of patients for statistical and research purposes.

The program was prepared in dBASE III PLUS language, Version 1.0 and compiled with Clipper Compiler, Summer 1987 (dBASE, Ashton-Tate Corp; Clipper, Nuntacket Corp.). It could be implemented with a hard disk or with 3.5 inches floppy disks. The MS-DOS was Version 3.30 (Microsoft Corp, Redmont, WA). When applicable, the commands mimicked Wordstar word processor rules (Wordstar International Inc., Novato, CA). The general outlay was kept easy in order to make it immediately intuitive to any user. The program was extensively used with several computers, with the idea to make it totally IBM-compatible. Install and setup features were added in order to allow tailoring of data to the user. The program was verified with more than 4000 entries. Provision was left for the implementation of the index for radiological diagnosis (American College of Radiology), if available. In the latter case, use of a hard disk was mandatory with RAM memory in excess of 450 K, but we found out that its use considerably slowed down the input process.

At the start the system prompts either for the main or the auxiliary programme. The main program allows data insertion, correction, and/or searching and printing. The auxiliary program takes care of features like printing of patients, copying of data, deleting of patients and code searching. The time required to introduce a new patient is approximately 1 min. The user is guided through each step with a visual display at the bottom of the screen.

Since the system was intended for public domain, usable with an IBM-compatible computer and an Epson-mode printer, the compiled program will be furnished by the authors, if a 3.5 inches floppy disk is enclosed with a written request.

Yours etc.,

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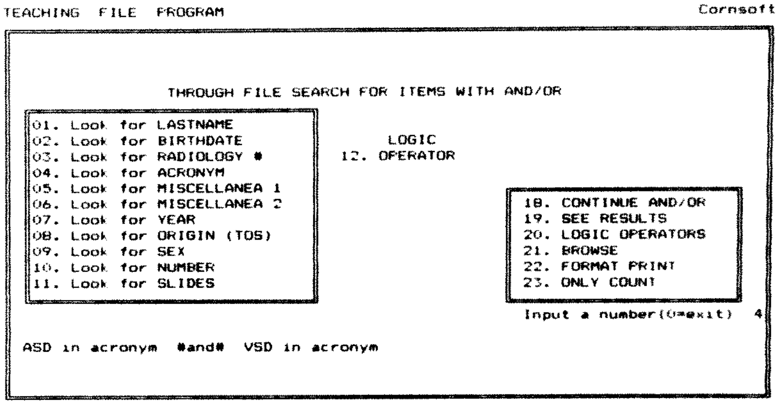
(Received 15 May 1991 and in revised form 6 September 1991, accepted 20 September 1991)



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TEACHING  FILE  PROGRAM                                              Cornsoft

                  THROUGH FILE SEARCH FOR ITEMS WITH AND/OR

 01. Look for LASTNAME
 02. Look for BIRTHDATE                  LOGIC
 03. Look for RADIOLOGY #            12. OPERATOR
 04. Look for ACRONYM
 05. Look for MISCELLANEA 1
 06. Look for MISCELLANEA 2                            18. CONTINUE AND/OR
 07. Look for YEAR                                     19. SEE RESULTS
 08. Look for ORIGIN (TOS)                             20. LOGIC OPERATORS
 09. Look for SEX                                      21. BROWSE
 10. Look for NUMBER                                   22. FORMAT PRINT
 11. Look for SLIDES                                   23. ONLY COUNT
                                                      Input a number(0=exit)  4

 ASD in acronym  #and#  VSD in acronym
```

Figure 1.

The use of MRI in the investigation of spinal cord compression

THE EDITOR—SIR,

Magnetic resonance imaging (MRI) already has an established place in the investigation of spinal cord compression (Chadwick et al, 1991), but is not widely available in district general hospitals in which, in contrast to academic centres, cost effectiveness is of paramount importance.

In the first 12 months following the installation of a Siemens Magnetom 1.0 Tesla MRI body scanner at Poole General Hospital;

a 600 bed general hospital incorporating a subregional radiotherapy centre, a total of 18 patients with compression of the spinal cord or cauda equina in the presence of known primary carcinomas were scanned. The data on these patients were analysed to assess the cost/benefit ratio, comparing MRI scanning using the whole body coil, so that patients do not have to be moved during the procedure, with conventional techniques, specifically plain X rays, isotope bone scans and myelography.

Six of the patients who were scanned would have been unable to tolerate myelography, either because of pain or debility and, of these six, MRI was essential in five of them to establish the limits of the disease to be incorporated within a suitable radiotherapeutic treatment field. All cases referred for MRI with axial neural compression were scanned successfully in that no other radiological investigations were subsequently required.

In seven cases additional information that would not have been apparent from other techniques was gained: evidence of dual level compression in four cases, demonstration of significant paraspinal disease in one case that required much wider palliative radiotherapy fields than would otherwise have been used, and the demonstration of concurrent hepatic and mediastinal metastases in two cases.

Assuming a mean cost per patient as follows (Poole Hospital data*)

MRI axial spine	£ 80.00
Plain X rays of whole spine	£ 41.00
Myelography	£ 160.00
Bone scan	£ 90.96

we concluded that MRI scanning in cases of axial neural compression (i) was 140% more cost effective per level demonstrated than myelography; (ii) is applicable to 30% more cases than myelography; (iii) has a significant "pick up" rate for abnormalities in other midline structures and (iv) is the investigation of choice in terms of information provided, economy and patient acceptability.

* Does not include allowance for fixed asset depreciation.

Yours etc.,

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(Received 21 August 1991, accepted 4 September 1991)

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The significance of patient weight when comparing X-ray room performance against guideline levels of dose

The Editor—Sir

In their letter on this topic, Hart and Shrimpton (1991) have highlighted a problem in the assessment of radiographic dose and comparison with the recently published guideline doses (NRPB, 1990). The problem is the variation in patient build and its affect on skin dose. They note that in the NRPB survey (Shrimpton et al, 1986) the range of mean patient weight for each room varied by about ±10 kg around an average of 70 kg.

During the last year we have initiated routine survey procedures for fixed radiographic equipment in the Lothian and Fife Health Boards' areas. These surveys are intended as a quality audit procedure to enable the radiology departments to assess whether doses are being adequately controlled. Entrance skin dose is measured using thermoluminescent dosemeter (TLD) for three examinations: chest (postero-anterior, PA), pelvis (antero-posterior, AP) and lumbar spine (AP, lateral, lumbosacral junction, LSJ). To ensure the most effective conduct of these surveys, a maximum measurement period of 1 week and a maximum number of 12 patients for each examination has been specified.

To date we have surveyed 12 examination rooms with measurements on 257 patients. For these patients the average weight was 69 kg with a standard deviation (SD) of ±13 kg. Hart and Shrimpton recommend that dose assessment be carried out for a limited sample of typical patients whose mean weight lies within 5 kg of 70 kg. The authors do not define what they mean by a sample of typical patients, but if we had chosen to restrict patients to within 10 kg of the average weight, we would only have made measurement on 56% of all the patients examined. This suggests that, if patients were selected by weight, the time period for each survey would have to be extended. This would be particularly restrictive for those rooms in which not many patients undergo the examinations studied. For these reasons we measure skin dose for all patients and correct for build.

The radiographer is asked to record the patient's height and weight, based on the patient's own assessment. The measured data are fitted to the following equation

$$\log(\text{dose}) = k_1 + k_2 \,.\, (\text{weight}/\text{height})^{1/2}$$

This relationship was chosen on the basis of a grossly simplified model of the patient as a uniform density cylinder with the attenuation of the radiation being a simple exponential. A standardized dose is interpolated from the data for an average patient: weight = 70 kg, height = 170 cm.

We have compared our results for this method for fit (A) with the linear relationship between dose and weight reported by Hart and Shrimpton (method B) for one particular radiographic view, AP pelvis, and for the six rooms in which more than five patients were examined. The data from these surveys are presented in Table I. The average patient weight was 67.3 kg which is less than the average for all patients surveyed, probably because of the higher number of females in this group (69%). It can be seen that the number in the weight range 60–80 kg is less than half the total. The average doses are presented for all patients in each room and for those in the restricted weight group. Uncertainties in the average doses are twice the standard error on the mean.

A good correlation between dose and weight was found with an average slope of 2.3% (minimum 1.0%; maximum 4.0%) of the dose per kg weight at a weight of 70 kg. This compares well with the data reported by Hart and Shrimpton (average 2.1%; minimum 0.7%; maximum 3.7%). The interpolated standardized doses from the two methods described above are shown in Table I. For these doses the uncertainty is the 95% confidence interval calculated from the linear regression fit to the data.

It can be seen that there is no significant difference between the dose derived by the four methods, but that the use of an unrestricted average dose is associated with a consistently higher uncertainly (average 32%) as expected. The standardized doses for method A

Table I. Results of surveys of entrance skin dose for AP pelvis examination. The uncertainties represent the 95% confidence intervals

Study number	6	10	12	14	15	16
Number of patients	6	8	12	9	12	12
Average weight (kg)	57	63	64	67	77	69
Average dose (mGy)	2.8	5.8	3.5	7.4	5.0	3.7
Uncertainty	13%	28%	41%	46%	28%	26%
Weight = 60–80 kg						
Number of patients	3	4	5	5	5	6
Average dose (mGy)	3.0	7.4	3.2	5.0	3.7	4.1
Uncertainty	21%	15%	22%	24%	14%	10%
Method A						
Standard dose (mGy)	3.1	6.4	3.7	6.8	4.0	3.6
Uncertainty	19%	15%	19%	28%	28%	12%
Method B						
Standard dose (mGy)	3.2	6.6	4.3	8.3	4.4	4.1
Uncertainty	20%	17%	22%	32%	39%	6%

are on average about 10% lower than for method B. This is because slightly different criteria are being used for standardization.

In any room, scatter in the results is to be expected owing to various factors which are not patient related. These include the precision of TLD measurements, the functioning of automatic exposure control devices or, if these are not used, the selection by the radiographer of the most appropriate factors, errors in setting the correct focus-film distance and variations in X ray output. Restriction to patients within a relatively small weight range, as suggested by Hart and Shrimpton, will be affected by the variations in height and by variations in the distribution of weight in the patient, which in part may be related to the patient's sex. It may be noted that the scatter of data for unselected patients is increased due to variations in the kV used for different sized patients.

For the restricted weight group our data indicate an average uncertainty of ±18% in the dose. This is for between three and six patients in each room. To reduce this uncertainty would require a larger number of patients within the specified weight range. Because of the difficulties of extending the time period of the survey sufficiently to get enough patients within this range, we have chosen to accept all patients (except children) up to the specified maximum number and to correct for build. For the two methods of standardization (A and B) the average 95% confidence intervals are ±21% and ±25%, respectively. There is little to choose between these methods principally because variations in patient height are very much less than the variations in weight. However, we have chosen to continue to use method A. The uncertainty associated with this evaluation of a standardized dose appears to give sufficient precision to make valid comparisons between rooms and with the guideline doses.

Yours etc.,

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Authors reply

The Editor—Sir,

It is gratifying to have so quick and detailed a response as given by Williams and Catling in their comments on our letter (Hart & Shrimpton, 1991). We agree that it is essential for patient dose measurements to be conducted efficiently whilst also yielding meaningful data. Indeed, the need for such local surveys has lead to the formulation of appropriate dosimetry protocols by NRPB in collaboration with the Institute of Physical Sciences in Medicine and the College of Radiographers which will be published shortly.

The stipulations followed by Williams and Catling of a maximum measurement period of 1 week and a maximum number of 12 patients for each examination were presumably necessitated by limitations in resources. Under more ideal circumstances, it would be wiser to take dose measurements on at least 10 patients for each examination even if a few weeks were needed, in order to achieve reliable results.

The main thrust of our letter was to provide reassurance that when one is comparing performance against a guideline dose, it is sufficient to determine the simple arithmetic mean entrance surface dose for a sample of patients as long as the mean weight of the group lies within 65–75 kg. Our suggestion of excluding extremely large or small patients was aimed at providing some control on the mean patient weight. Williams' and Catling's assumption that we might have meant selecting only patients with weights between 60 and 80 kg is more restrictive than we intended and would inevitably lead to rejection of significant numbers of patients, as evident from the histograms in Fig. C2 of NRPB Report R-200 (Shrimpton et al, 1986) where individual patient weights range from 25 to 150 kg. On the other hand, it would seem prudent to exclude from routine measurements some of the relatively small numbers of patients on the fringes of these distributions. Dose data for which the mean patient weight lies outside the range indicated above can be adjusted simply by using the typical trends given in Table II of our letter.

In carrying out patient dose surveys, it is important for the investigator not to forget both the overall levels of uncertainty inherent in such measurements and also the philosophy behind the guideline doses: they are intended to promote the important process of optimization in radiography by encouraging staff to make critical examinations of their techniques and by acting as investigation levels to aid the early identification of departments with particularly poor practice.

Yours etc.,

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(Received 19 September 1991, accepted 3 October 1991)

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Scattered X-ray intensities from fluoroscopy units

The Editor—Sir,

We refer to the protection afforded by multileaf Pb aprons on fluoroscopy units and would like to offer our own illustrative example of the importance of such measures in shielding against scattered radiation. Our concern lies with an incident that occurred in a hospital and which involves a fluoroscopy unit (a Siemens Gigantos with a 100 kW multipulse generator capable of delivering 1000 mA and 150 kVp) that was operated in the absence of its protective Pb aprons. Figure 1 shows the image of a gastrointestinal tract (using Curix Agfa Gevaert X-ray film and a $CaWO_4$ normal-speed screen combination) and a superimposed forearm (not that of the patient).

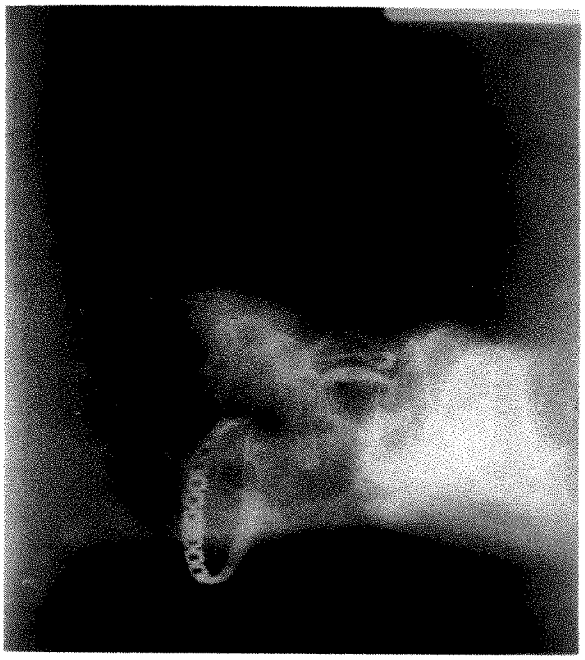

Figure 1.

Reconstructions from this isolated incident, indicate this to be a Compton-scattered image of the forearm of a registrar who (i) was holding under her arm an already exposed cassette ready for processing and (ii) was momentarily adjacent to the patient (some 80 cm distant from the midline of the table top) during a further radiographic exposure. Using a water-filled tank to simulate the scattered X-ray intensity due to a patient we have subsequently obtained, under similar situations, an image of an inert object and measured an entrance dose at the image receptor of approximately 5 μGy (using a PTW D14/DL4 dosemeter with 1000 cm^3 ion chamber) for exposure settings 85 kVp, 5 mAs, 10 ms. In this respect Dendy and Heaton (1987) mention that in order to produce unit optical density in film-screen combinations (presumably with conventional screens and use of a grid) entrance doses of 10 μGy are typically required. It is conceivable, owing to uncertainty in the exact position of the registrar, that an entrance dose of up to 10 μGy may actually have occurred. With the Pb apron in position we were unable to record exposures.

Yours etc.,

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Book reviews

Interstitial Brachytherapy: Physical Biological and Clinical Considerations. By L. L. Anderson, R. Nath, K. A. Weaver, D. Nori, T. L. Phillips, Y. H. Son, S. Chiu-Tsao, A. S. Meigooni, J. A. Meli and V. Smith, pp. xx + 360, 1990 (Raven Press, New York), $122.00.
ISBN 0–88167–581–4

This book is produced by the Interstitial Collaborative Working Group in the United States, with contributions from 10 authors from the fields of radiotherapy and medical physics. The book aims to cover the clinical, biological and physical aspects of interstitial therapy. There are 11 sections to the book covering radioactive sources, planning an implant, radiobiology, clinical instrumentation, clinical procedures, source localization, dose computation, dose evaluation, quality assurance, radiation protection and future directions of brachytherapy.

Each chapter is short and concise and gives practical guidance for both clinical and physical procedures. Section five, the section on clinical procedures, covers the application of interstitial implants to a large range of sites in the body and it is particularly comprehensive. In this section guidance is given on tumour localization, choice of radionuclide, how the treatment should be planned and how the implant should actually be positioned. The directions are quite specific and would be very helpful to trained practitioners of interstitial therapy. It is not a book, however, for trainee radiotherapists or practitioners with no prior experience of interstitial implants. The book is concise, well written and easy to read and is well produced with good diagrams and radiographs of implants.

In general, the field of brachytherapy is one which is moving forward rapidly, with the introduction of high dose rate systems and microprocessor controlled source localization. I think that this book, with its emphasis on treatment with iridium, iodine 125 and radioactive gold is likely to remain relevant to interstitial practice for many years. It would certainly have a place in any department involved in interstitial implant therapy.

P. Blake

An Introduction to Radiobiology. By. A. H. W. Nias, pp. ix + 346, 1990 (John Wiley & Sons Limited, Sussex), £17.50.
ISBN 0–471–92756–2

To attempt an introduction to "radiobiology", bearing in mind the diversity of topics covered by this word and the vast literature now available, is no mean task. I think Professor Nias has succeeded admirably. Inevitably, one expects, and indeed finds, some bias towards those topics in which the author has principal interest. In this case, that bias, cellular radiobiology, has considerable advantage since a good understanding of basic cellular behaviour and kinetics is really very necessary for the interpretation of many radiobiological phenomena, and it is just this understanding which is often lacking, and which in the past has often led to some curious explanations.

The book consists of 20 chapters each with a short bibliography and concludes with some suggestions for further reading, a glossary of terms and an index.

The chapters build up a logical sequence, starting with cell biology and proliferation kinetics. After having discussed the properties of ionizing radiations, their effects upon cells, the damage and its repair and modification are discussed. This sets the scene for looking at the practical application of radiation to therapy of cancer and the rationale that underlies the various regimes of dose fractionation and protraction that are in current use. The book concludes with a few chapters on environmental hazards, risk assessment and radiation protection.

There are plenty of useful and well chosen figures and graphs and some valuable summary boxes emphasizing main conclusions scattered throughout the text. The whole is very readable, though some knowledge of basic physics, chemistry and mathematics is required. This is undoubtedly one of the better introductions to the subject which I have read, and I would certainly recommend it not only to beginners but also to mature students of the subject.

J. R. K. Savage

Cranial Meningiomas—Diagnosis Biology and Therapy. Ed. by G. B. Bradac, R. Ferszt and B. E. Kendall, pp. ix + 154, 1990 (Springer-Verlag, Berlin), DM 248.
ISBN 3–540–17682–9

This monograph by authors from Germany, Italy and the United Kingdom, is a very complete treatise on the subject of cranial meningiomas, but as the title indicates, spinal tumours are not covered. The inclusion of Dr Brian Kendall as co-editor and Dr John Stevens from the National Hospital for Nervous Diseases, is a tribute to their important joint contributions to the literature on meningiomas.

Separate chapters are devoted to the clinical and pathological features of meningiomas, the skull radiograph, computed tomography, magnetic resonance imaging and angiography. Further chapters then deal with meningiomas, in particular anatomical locations with one chapter on peritumoural oedema.

As is usual with Springer publications, the standard of the illustrations is extremely high and typographical errors few. The reference list is at the end of the book and is referred to in the text by means of numbers, which in my opinion promotes the fluency of the chapters and quite simply makes them easier to read.

The work concludes rather interestingly, with a chapter of 11 pages on embolization (albeit illustrated with many radiographs) and a final chapter of only six text pages concerning surgical aspects. This underlines the fact that this book is concerned mainly with the radiological aspects of meningiomas. In keeping with this, the book is recommended primarily to departmental libraries serving neuroradiologists, but neurosurgeons and neurologists will also find it of interest. The high price and specialist nature of the book may deter the individual purchaser.

P. Butler

Angiocardiography in Congenital Heart Malformations. By B. Soto and A. D. Pacifico, pp. 669, 1990 (Futura Publishing Company, USA), $175.00.
ISBN 0–87993–336–4

At a time when most textbooks on cardiac imaging are concentrating on the newer techniques and, in particular, non-invasive methods, it is rather unusual for a new textbook on cardiac angiography to emerge. The University of Alabama is a world-renowned centre for congenital heart disease and the great experience of a cardiac radiologist and a surgeon has been combined in producing this impressive volume.

The first chapter deals rather briefly with angiographic techniques, but this is followed by an excellent account of normal cardiac morphology. The remainder of the book comprehensively covers the range of congenital heart disease which is sensibly arranged using the now well accepted modern classification. For each malformation, the format consists of a definition, followed by a detailed account of morphology, illustrated by photographs of pathological specimens. Though these are well chosen and clearly labelled, they remain two-dimensional and I wondered how valuable these will be to cardiologists and radiologists as opposed to cardiac surgeons. Dr Bargeron pioneered axial angiocardiography from Birmingham, Alabama and it is no surprise that his cineangiography images of the highest quality extensively illustrate the subsequent descriptions of angiocardiography, even if the role of much angiography is now being replaced by echocardiography. I think all the cine images are well produced and clearly illustrated making this an impressive atlas of congenital heart disease. In the text there are, in addition, clear and detailed descriptions of the angiographic findings. Where necessary, diagrams are used to illustrate complex lesions and in a few instances, the chest X-ray findings are related to angiography.

This book is a specialized text and is not a general account of congenital heart that will be useful for general radiologists and radiologists in training. Rather, it is a very comprehensive and beautifully illustrated account of angiocardiography in congenital heart disease that will, I am sure, become a classic and be essential for anyone actively involved in paediatric cardiology.

J. F. REIDY

Bone Marrow Transplantation in Children. Ed. by F. Leonard Johnson and Carl Pochedly, pp. xxi + 529, 1990 (Raven Press, New York), $150.00.
ISBN 0-88167-575-X

As with other forms of organ transplantation the subject of bone marrow transplantation has aroused considerable public interest and remains an emotive topic. The expense, both in terms of supportive care and patient morbidity must be justified by clear evidence of a therapeutic advantage. This timely overview by several leading practitioners from North America considers, in detail, the main aspects of both bone marrow transplantation techniques and their application to a variety of malignant and non-malignant conditions in children.

Of particular interest are the introductory chapters, outlining the history of marrow transplantation and a useful overview of the basis of the histo-compatibility barrier. Inevitably with such a multi-author volume there is some overlap, particularly with regard to describing the clinical and pathological features of graft *vs.* host disease. This area is covered in at least three separate chapters and some rationalization would have been advantageous.

In view of the widespread use of cyclosporin A, a little more information on the practical details of managing patients with regard to the importance of monitoring drug levels, the different schedules used, drug interactions and drug toxicity would have been of value.

The role of autotransplantation in acute lymphoblastic and acute myeloid leukaemia is dealt with somewhat briefly and some discussion about potential immune modulation post autograft, such as induction of graft *vs.* host disease or cytokine therapy would have been of interest. The section on autotransplantation for solid tumours describes the limited experience in several paediatric tumours. In view of the very extensive world experience with neuroblastoma, a separate chapter considering this disease might have been appropriate. Instead there is a specific chapter for the application of this treatment approach to sarcomas, reporting largely the experience of a single centre.

The need or otherwise of total body irradiation prior to transplantation is an important issue and the difficulties associated with this are highlighted in a review of late effects due to this treatment modality. Adverse effects on growth, endocrine function and most organ systems are detailed and must surely lead us to try and devise high dose regimens with fewer late effects before introducing this treatment modality on a wider scale.

In conclusion, this book provides an excellent overview for those involved in high dose chemoradiotherapy with bone marrow rescue, or for paediatricians who wish to learn a little more about what awaits their patients when referred to a specialist transplant centre. Bone marrow growth factors and improved high dose regimens may reduce morbidity in the future and it is hoped that a further edition may be able to concentrate less on acute and late morbidity and more on therapeutic success.

C. R. PINKERTON

BIR Bulletin

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Report of the Summer Meeting of the Welsh Branch of the British Institute of Radiology

The Cliff Hotel, Gwbert on Sea, Cardigan *7th–8th June 1991*

By David A. Robinson

This summer's meeting was organized by the Carmarthen radiologists and held in scenic surroundings overlooking the Teifi estuary. At an informal dinner on the Friday evening, we were pleased to welcome the President of the BIR, Professor C. A. F. Joslin and his wife. The scientific meeting took place in the hotel on the Saturday morning. At the business meeting Professor Joslin spoke about the important work of the Institute and gave an overview of the role it may play in the future development of diagnostic imaging. Dr Neils Powell from Swansea was elected the new Chairman of the Welsh Branch and Dr David Robinson from Abergavenny was appointed Secretary.

The scientific programme was opened in inimitable style by Dr Charles Bartlett, Consultant Radiologist at West Wales Hospital, Carmarthen. He described his experience of the treatment of urethral strictures with balloon urethroplasty. He briefly reviewed the common causes of urethral strictures and gave an amusing historial resume of the various treatments used in the past. He then went on to describe his technique of using a 6 mm balloon mounted on a 5 French catheter to dilate six cases of urethral strictures. The majority of these were inflammatory strictures of the membranous/penile urethra, all of which had done well at 6 monthly follow up. There were two failures, one of which was a difficult post-traumatic stricture where this technique may not be particularly suitable. To the surprise of the male members in the audience, he assured them that the technique was largely painless with no significant complication rate. He concluded by suggesting that no hollow tubular structure within the human body was now immune from the attentions of the interventional radiologist.

The second talk was given by Dr Shelley Renowden, Lecturer in Radiology at the University of Wales College of Medicine. She provided evidence to show that this was a common consequence of renal biopsy, occurring in up to 16% of cases. She reviewed the previous methods of diagnosis, largely angiographic, and then put forward a persuasive case for the use of a combination of colour/pulse Doppler in the diagnosis of these lesions. She then described the typical features: increased arterial diastolic velocity, tissue vibration, reduction of the resistive index and increased venous pulsatility with turbulence at the site of the fistula itself. The prognosis for these lesions was variable with many superficial lesions closing spontaneously, though some of the deeper lesions where there was evidence of significant hypertension, or reduction of renal function, had to be treated with surgery or embolization.

The third talk of the morning was given by Dr. Rob Parry, Lecturer in Radiology at the University of Bristol. He described some of the preliminary results obtained by the Bristol group on intraarterial Doppler evaluation of percutaneous lower limb angioplasty. Most people involved in peripheral angioplasty will be familiar with the problem of lesions with apparently similar anatomical results following dilatation leading to very different clinical and functional results. Dr Parry described the work as an attempt to provide the missing link between anatomy and function in an effort to predict which lesions were likely to recur. The first half of the presentation reviewed the painstaking work of validation that had been performed on the three French Miller catheter with a 20 MHz Doppler crystal mounted at its tip. He emphasized the importance of setting the sample volume at least 6 mm away from the catheter tip to avoid turbulance artefacts caused by the catheter and he also covered the problem of side branches. The best velocity profiles were obtained when the catheter was placed centrally within the vessel lumen. He discussed the theoretical problems of alterations in proximal flow and distal vascular resistance, which may mask the effects of the lesion itself and gave a brief overview of the algorithms available for correcting for alterations and proximal flow. He concluded with the clinical results of the assessments on post-angioplasty patients and suggested

Continued overleaf

that lesions with a pulsatility index of >2 and a resistance index <8 tended to have a good prognosis. The main advantage of the technique over external pulse Doppler information was the quality and reliability of Doppler information obtained.

Following the coffee break Dr Gerald de Lacey, Consultant Radiologist at Northwick Park Hospital, gave us a fascinating and erudite presentation on his work on audit and clinical review, with particular reference to accident and emergency radiology. He outlined audit processes which could be set up in a minimal period of time in any busy X-ray department and he emphasized the importance of keeping the process relatively simple. He then described in more detail the ongoing research on both the clinical impact and social consequences of plain film usage in an accident and emergency department. He described the early work where figures had shown that the incidence of patients radiographed varied dramatically from one department to another (30%–70%) for no obviously good reason. He then outlined the measures used in his department to reduce a number of unnecessary radiographs and emphasized the fact that printed guidelines or booklets have to be continually reinforced with posters and educational material. The most interesting section, however, provided fairly firm evidence for what radiologist have always known, that the vast majority of radiographs are performed not for any proper medical indication, but to placate the patients. X-rays often acted as a substitute for good practice and reassurance. The questionnaires had also shown that people who expected radiographs were often disappointed and had a longer period of minor adverse symptoms following trivial head injury. His research confirmed that different groups of casualty officers used radiographs in different ways, with locums and those not on rotational schemes having a far more profligate attitude than those who were on surgical and GP training schemes. This, it was suggested, was related to levels of interest, motivation, confidence and clinical judgement. He underlined the difficulties of affecting any actual reduction in radiographs performed, but underlined that the potential savings, both in radiation dose and financial cost, could be considerable.

The last talk of the morning was given by Lindsey Carver from IGE Medical, who gave an overview of the current developments in MR imaging. It was clear that MR angiography has finally come of age, although it would appear that both time of flight and phase contrast both have a part to play in different vascular situations. She also described the various methods that have been used to improve both the quality and acquisition time for imaging with very rapid sequences now available for developing both T1 and T2 contrast. Advances in the software have also been matched with high strength gradient coils and new quadrature acquisition coils. Most exciting of all, the new phased array coils capable of producing high resolution images over a large field of view. Work continues on echo planar imaging, which appears to have been waiting in the wings from the earliest days of MRI and, although real time acquisition and display are now a reality, poor spacial resolution remains a major drawback. Changes in magnet design and shielding were also reviewed, with active shielding now a relaity at mid and low fields, though still somewhat problematic at high field. Towards the end of her talk she gave a fascinating insight into the possible commercial direction of MRI systems directed at a particular application, such as cardiac or orthopaedic imaging, with software specifically geared to the particular clinical problem in hand. Her excellent overview in many ways served only to increase the frustration of those of us who are still struggling to acquire even the most basic form of MRI, let alone state-of-the-art technology.

MEWS HOUSE
10 Cavendish Mews
North
London W1

The Institute is pleased to announce that its newly refurbished Mews House is now available to rent.

This elegant property is situated in Cavendish Mews North in the heart of London's West End. It is conveniently located for both Harley Street and the major hospitals.

Briefly the property comprises:

- Spacious lounge / diner
- 3 bedrooms (master bedroom ensuite)
- Family bathroom
- Luxury fitted kitchen
- Integral garage
- Delightful patio / sun terrace

It is anticipated that the property will be rented on a company let basis and on competitive terms to be negotiated.

If you require further details or wish to view the property please contact: Tony Hudson, Administration Manager by telephone 071-580 4085 or by fax 071-255 3209.

Obituary

Norman Veall DSc, CPhys, FInst Phys, Hon MRCP

24 May 1919 – 30 August 1991

Norman Veall's career reflects the mind of a man who refused to be chained by convention. He always considered the whole of medical physics his province and justifiably can be ranked among the founding fathers of this discipline.

His academic studies were interrupted by the war. He spent the war years at Chalk River in Canada working on the "Tube Alloys" project but continued his academic work as an external student and was awarded a BSc in Physics and Chemistry by the University of London in 1943.

Back in England he joined the Radiotherapeutics Research Unit at the Hammersmith Hospital under the leadership of LH Gray in 1946. There he applied his many natural skills (he was a very good glass blower and not a bad painter) to the development and improvement of radiation detectors and their application to the solution of physiological problems in collaboration with his many medical colleagues. It was also here that he contributed to the development and refining of the tracer methodology which he then applied with great success to problems which varied from placental localization to blood flow in tubed pedicles. His scientific output was large and covered many fields. His publications during this period could be found in journals ranging from the BJR to the British Journal of Plastic Surgery. Among this periods' achievements one can mention the first thyroid radioisotope scan obtained by placing a Perspex graticule over the gland and plotting the counts from a collimated Geiger counter in each square and a simple whole body scanner made by attaching Geiger tubes to the framework of a bed screen!

Norman Veall's outstanding contributions stemmed from his lasting interest in the application of radioactive tracer techniques in the solution of clinical problems, and this led to much fruitful collaboration with medical colleagues in many diverse topics. With Mollison and others, he developed methods of measuring tissue blood volumes and applying them, for example, to measurements in newborn children. His work on tissue circulation with Barron, especially applied to problems in plastic surgery, brought recognition as consultant physicist at the Plastic Surgery Centre, Salisbury, whilst his work on placental localization with Browne led to a consultancy at the Institute of Obstetrics and Gynaecology.

In 1953 Norman moved to Guy's Hospital as Senior Research Fellow in the Medical School. There he continued the fruitful collaboration with his clinical colleagues which culminated in the development of the Xe-133 inhalation technique for measuring cerebral blood flow, and in the publication, with Vetter, of *Radioisotope Techniques in Clinical Research and Medicine*. The book was translated into several languages and became the standard reference on the subject.

By the end of the 1950s his reputation in clinical physics became international and he was appointed visiting professor in several developing countries. The setting up of nuclear medicine facilities in the developing countries was close to his heart and his penchant for devising simple, robust equipment proved of great value to the IAEA's projects in the third world.

In the 1960s Norman rejoined the MRC as a member of the External Scientific Staff based at Guy's and became involved in the planning of the Clinical Research Centre. In 1970 his outstanding contributions to nuclear medicine were publicly recognized through the award of a DSc by the University of London. In the same year he was appointed head of the radioisotopes division of the CRC and honorary head of the Radioisotopes Department at Northwick Park Hospital.

In spite of the increase in administrative duties he continued to produce much innovative work especially in the fields of renography, bone blood flow and inherited metabolic diseases. At the same time he continued his collaboration with the IAEA, contributed substantially to committees and task groups of ICRU and ICRP and later ARSAC and was heavily involved in the teaching of nuclear medicine to clinicians.

Although Norman retired in 1984, he continued his association with the CRC and contributed substantially to the development of labelled neuroleptics for the study of their role in mental illness.

Earlier this year he had a stroke which made him unable to travel. He was still, however, always willing and usually more than able to give advice over the telephone. A second stroke in August robbed medical physics of one of its most dedicated and innovative practitioners. He leaves his wife Kathleen, son Leonard and daughter Jacqueline, to whom we express our sympathy.

His friends and colleagues

UK - USSR Medical Exchange Programme

THE UK-USSR Medical Exchange Programme, the only organization of its kind in the EEC, was founded in 1984 to further the exchange of medical knowledge and of health care professionals between the two countries. At first the exchange was almost entirely one way. Now both small and large groups of soviet health care professionals visit Britain under the programme.

When, in 1987, the then Health Minister Academician Yevgen Chazov introduced "Glasnost" into the soviet health service, the State of Health Provision outside the elite institutes became widely known for the first time. This meant radical changes in approach and since then many groups have visited institutions which before they would never have been permitted to see.

The programme has responded to the newly identified needs by developing exchange fellowships in order that soviet professionals can have the chance to master western advances in patient care, and so make up for their long years of isolation. The idea is to train people who can return as trainers themselves, and so pass on their knowledge.

Support for the programme has come from both public and private sources, and recently the BIR became a collegiate member of the scheme. On 3rd September 1991, the UK-USSR exchange programme hosted a Conference on "Medical Exchange, Aid to and Trade with the Soviet Union", which was attended by representatives from the Institute, as well as senior representatives from other medical academic institutions, Welfare Agencies, the DOH, Industry and the Press.

The morning session was chaired by Sir Sigmund Sternberg, with the opening address provided by Stephen Dorrell MP, junior health minister, who emphasized the priority importance that the government attaches to trade and public health within the USSR, and hinted at the possible availability of funds for this, through the "know-how" scheme. Further speakers then detailed the impoverished and chaotic nature of soviet health service provision, based upon their own personal experiences. These included Ralph Land, Chairman of the Anglo-Soviet working group on information technology.

John Pendlebury from Coopers and Lybrand described the problems facing the soviet health care system. These include high infant mortality (two and a half times higher than the USA), poor life expectancy, the highest abortion rate in the developed world, AIDS (one and a half million cases anticipated by the year 2000), the unavailability of essential medicines, insufficient funding (3% of GDP) and low medical salaries (in many cases less than unskilled soviet workers).

In the afternoon session the meeting split into "Workshops", to coordinate activities in such areas as primary health care, child health and Chernobyl-related illness.

Perhaps the most important single area in which the UK and its academic institutions can contribute is in education and training of health care personnel, although direct aid in the form of basic medical equipment would also be of considerable value in the short term. There is also a wide-spread lack of meaningful health care statistics within the USSR to aid the provision of future resources, and the UK, with its advanced information technology systems applied to medicine would also be able to assist in this field.

The UK-USSR scheme has the full support of the Council of the BIR. The Institute, with its strong academic tradition and multidisciplinary nature within the radiological sciences is probably well-placed to assist the soviet health care system through information and educational exchange. Any member of the Institute who knows of an exchange scheme for soviet (or Eastern European) health care personnel in their locaility, or would like to establish one, are encouraged to write to Dr N.W. Garvie, at the BIR.

N.W. Garvie

Company profile

Wardray Products Limited and J. Wardley (Holdings) Limited

IT IS highly unlikely that John Wardley, arriving in London in 1909 as a master carpenter, can have imagined that his formation of a business producing butterfly cases would one day result in an organization manufacturing and installing X-ray protection products throughout the UK and overseas.

A chance remark to a friend gave him the first order to bond sheet lead to a piece of plywood and was the start of the Wardley family's activities in radiation shielding which now spans nearly 60 years.

Today, Wardray Products Limited and J. Wardley (Holdings) Limited occupy over 12000 square feet of factory, warehouse and offices on a modern site in Thames Ditton, Surrey.

Using the latest machinery and equipment they manufacture not only a wide selection of structural X-ray protective products (doors, screens, panelling, partitions etc) but also flexible protective clothing including the well known ULTRAFLEX X-ray aprons.

The business continued to expand following an association with Fuji covering film distribution and the servicing of their highly regarded processing equipment in London and South East England. The organization's engineering expertise combined with our joinery manufacturing has also resulted in a number of supporting products including storage units and water filter boards.

More recently, again using their own manufacturing skills, Wardray has embarked on a design, production and installation programme to provide RF cages for MRI equipment.

This totally UK constructed system offers exciting prospects for the future of this family run business which, with an exceptional team of works, sales, servicing and office staff, will continue to give not only well designed, high quality products but also a reliable, helpful and friendly service.

Dornier Medical Systems UK

Dornier in the UK

Deutsche Aerospace along with Mercedes Benz and AEG form part of the giant Daimler-Benz organization of Germany. One division of Deutsche Aerospace is Dornier, a company whose interests are as diverse as the manufacture and service of aeroplanes through to the development and production of medical equipment.

Dornier Medical (or more correctly, Dornier Medizintechnik) has been producing and selling the Dornier range of lithotripers in the UK for a number of years and launched its latest product — the Dornier A1 series of ultrasound systems at the end of 1990 at the British Medical Ultrasound Socity meeting in Harrogate.

This system has been jointly developed by Dornier and Acoustic imaging of the USA, a company 87% owned by Dornier and is, we believe, the most advanced ultrasound system available today, drawing on the extensive transducer expertise within acoustic imaging the vast technological and financial resources of Dornier.

During the first half of 1991, Dornier gained exclusive rights to promote the Endosonics "CATHSCANNER" system for intraluminal computed sonography. This unique system employs a co-axial catheter combining the balloon and miniature phased array 20 MHz ultrasound transducer.

The Company believes in offering the highest level of customer support with top quality service back up commensurate with the supply of such high definition ultrasound imaging systems.

BIR T-shirts and Ties

BIR T-shirts are available to members at £7.50 each (including postage) and are black or navy blue with a white skeleton on the front and back. BIR silk ties are £15.00 each (including postage). They are navy blue and carry the rays from the Institute's logo, in gold. Please send a cheque payable to the BIR with the order.

PRESS RELEASE

Radiographers' Dotty Scheme

Enstar Red Dots have been produced to overcome the possible reluctance of some radiographers to tag suspect radiographs in casualty departments and elsewhere. Tagging with red dots helps casualty officers at the same time as giving greater job satisfaction to radiographers.

With Enstar Red Dots the question mark on the dot indicates to the casualty officer or radiologist that the radiographer may have identified an abnormaility, and nothing more. The question mark indicates possibility, not fact, and this removes the fear of legal liability for the diagnosis from the radiographer.

Enstar Red Dots are supplied in dispenser boxes of 1000 and are printed with non-toxic inks onto white self adhesive labels. They are just one of a wide range of Enstar self adhesive labels produced for hospitals and the medical services.

A New Partnership

The Somerset MRI Centre and Philips Medical Systems are pleased to announce the establishment of a new partnership in MRI. The centre has chosen to place an order with Philips for the supply of their new Gyroscan T5/XPA.

The Somerset MRI Centre and Philips will be closely cooperating in a clinical partnership that will establish the UK benchmark for MR image quality.

The Gyroscan T5/XPA, based on the winning technology of the original T5 system, is an 0.5 Tesla scanner with no compromise on performance, providing all the advantages normally expected with a 1.5 tesla system.

Freestyle scan planning with multiple coils, homogeneous off-centre imaging facilities, 3D volume investigations with real-time multiplanar reformatting, fast-scan imaging for motionless abdominal applications and MR angiography are all standard features on the T5/XPA system.

As a recognized centre of excellence, Somerset MRI is part of the Kerland Clinic, a foundation that was set up to benefit brain-damaged children. Proceeds from patient scans at the MRI centre go towards funding the clinic. The centre itself, which has been operating since August 1986, is a charitable organization providing a diagnostic imaging service for national health and private patients on a local, national and international basis.

In the Gyroscan T5/XPA, the centre will be acquiring state-of-the-art technology.

Dr Andrew Longstaff, Consultant Radiologist, Somerset MRI Centre, Ms Annette Schmidt, MRI Sales Specialist, Philips Medical Systems, Dr Tim Lewis Consultant Neuroradiologist, Somerset MRI Centre, Mr Peter Sharpe, Managing Director, Somerset MRI Centre, Mr John Coldwell, Product Manager, MRI, Philips Medical Systems, Dr Peter Cavanagh, Consultant Radiologist.

BIR Company Subscriber Scheme

The BIR company subscriber scheme is aimed at all companies with an interest in radiology and allied sciences.

For an annual subscription of £300 p.a. member companies are offered an attractive benefits package. To find out why your company should join the leading edge companies listed below, please contact Mr Tony Hudson, Administration Manager, British Institute of Radiology, 36 Portland Place, London W1N 4AT. Tel: 071-580 4085.

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Contact Mrs P. Dhanani, Medical Sales.

SPECIAL REQUEST

The Muhimbili Medical Centre in Dar-es-Salaam, a university teaching hospital, has requested current radiology textbooks. This department runs the only school of radiology in the country, but it is very difficult to obtain books and those available are very expensive. A list is available on request, but they would be grateful for any titles. If anyone has, or knows of, copies of such books could they please let me know at 12 Turner Close, London NW11 6TU. Collection in north and central London can be arranged.

With thanks, Anne Savage, Honorary Secretary Friends of Overseas Hospital

PRESS RELEASE

Cementing the Siemens Service

Mr. F Graves, Chairman of the South Birmingham Health Authority, recently took part in a ceremony at the Royal Orthopaedic Hospital, Birmingham, to mark a further milestone along the road to the completion of the hospital's new MRI unit. A contract for the purchase of a Siemens Magnetom magnetic resonance scanner was signed by representatives of the hospital in February 1991.

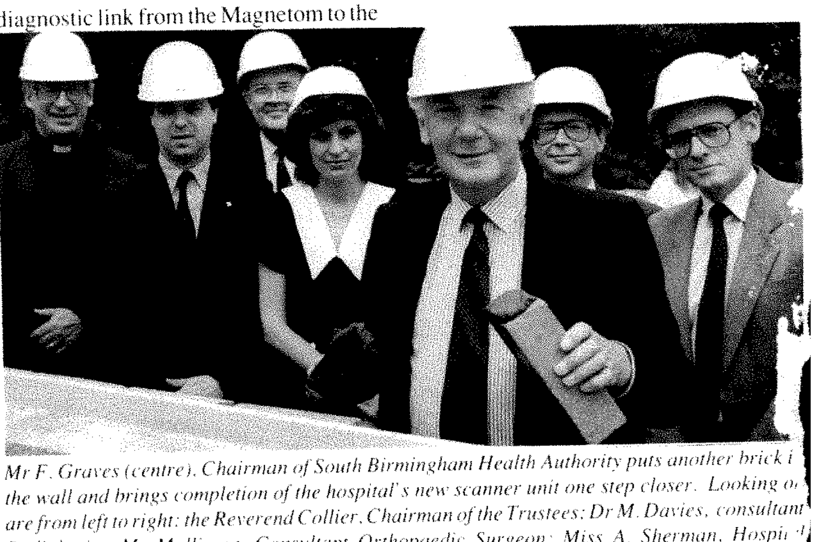
The Siemens Magnetom 42 SP/AS is optimized for a broad range of applications with particular emphasis being placed on orthopaedic imaging, a field in which the scanner's high resolution and ability to produce "thin slices" are vitally important. It is also possible to use the scanner to acquire 3D volume sets, a factor which will have a considerable bearing on both the clinical and research work which will be carried out at the hospital.

The high signal-to-noise ratio offered by the Magnetom means that most examinations can be carried out more quickly than with equipment having lower field strength magnets. This speed of operation ensures that examination times can be reduced, allowing optimum use to be made of the scanner.

Siemens will also install a remote diagnostic link from the Magnetom to the company's service centre in Sunbury-on-Thames, Middlesex. This link will enhance the rapid service already offered by the company's regional office in Birmingham and will connect the hospital's scanner to other Siemens' MR sites throughout the world, assisting communication for research projects.

The Magnetom to be installed at the Royal Orthopaedic Hospital will be equipped with a new 1 Tesla "Active-Shield" magnet. The magnet is shorter in length than those currently available — creating a more patient friendly environment — and is considerably lighter than magnets of comparable performance. A further benefit claimed by the company is that a patented principle makes it less sensitive to moving ferromagnetic objects.

Developments of the "Active-Shield" magnet resulted directly from the collaboration between Siemens Medical Engineering and Oxford Magnet Technology Ltd (OMT). OMT — a company in which Siemens holds a majority stake — exports 97% of its products and is the largest manufacturer of magnets for human body MR imaging in the world. The Eynsham based company recently won a Queen's Award for Technology.



Mr F. Graves (centre), Chairman of South Birmingham Health Authority puts another brick i the wall and brings completion of the hospital's new scanner unit one step closer. Looking o are from left to right: the Reverend Collier, Chairman of the Trustees; Dr M. Davies, consultant Radiologist; Mr Mulligant, Consultant Orthopaedic Surgeon; Miss A. Sherman, Hospi Manager; Dr N. Evans, Consultant Radiologist and Mr E. Orme, Regional Manager, Sieme Medical Engineering.

PRESS RELEASE

CRONEX*ly reduced radiation doses

REDUCTIONS in skin radiation doses of up to 60% were observed at West Suffolk Hospital, when the busy X-ray department switched to Du Pont CRONEX* Super Rapid screens

East Anglia is the first region to formalize the measurement of skin radiation doses, based on the recommendations by the National Radiological Protection Board (NRPB) which gives guidelines on entrance doses for a range of radiographic views. The procedure involved the quick and simple use of themoluminescent dosemeters and enabled a comparison of X-ray doses in departments throughout the region to be made, identifying those departments where dose reductions were required. The positive approach adopted by the radiography staff involved was praised by Ms P. Wade, the medical physicist in charge of the study.

"It is important to have the cooperation of everyone, as well as good feedback and a willingness to react to the results," she said.

"The survey has allowed us to quantify the situation, and a number of radiographers have gone back and reviewed their practices," Ms Wade said.

"We were not aware before the survey that our dosages were so high," said Mr Laurie Waldron, Superintendent Radiographer in the department, "so we realized that we had a lot of work to do." Changing from Quanta Fast Detail to Quanta Super Rapid screens in combination with existing CRONEX* 10L film has means an increase in imaging speed from 200 to 600 and a major reduction in dose, without significantly reducing the image quality, an important factor in the survey.

"We are delighted with the new equipment," said Mr. Waldron, "as we are now giving half the NRPB reference dose for the UK, we have moved into the top one-third of departments in the region, and all we changed was one item: the screens.

"More patients are keen to know what dose they are getting," he said, "and the shorter exposure times are particularly good for children, not only because of the reduction in dosage, but also because it can be difficult to keep children still for long."

*Trademark

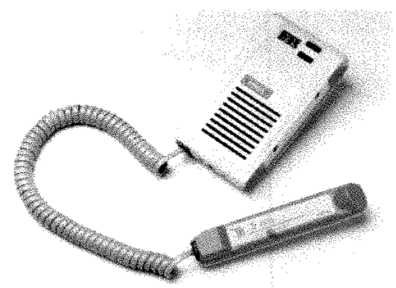
Digital Doppler on the market

IMEX Medical Systems introduces the Pocket-Dop 3TM, the most significant advance in hand-held fetal Dopplers in 12 years.

The new Pocket-Dop 3 is the first hand-held Doppler to incorporate autocorrelation, a sophisticated pattern recognition technique to help physicians quickly find and accurately track the complex signal of the fetal heart. Plus, an exclusive averaging mode provides the average heart rate on command in large, easy-to-read digital numbers.

Other innovative features include the wall mount or countertop "Smart Charging System" so that the Doppler [illegible] ready when you need it. A convenient magnetic probe holder holds the probe gently, but firmly, to the side of the unit. Removing and replacing the probe switches the unit on and off. As always, Imex offers interchangeable multi-frequency probes to meet all obstetrical applications, a 5 year parts warranty, comprehensive manuals and a customer service hotline.

Imex Medical Systems, Inc. is a leading US manufacturer of obstetrical Dopplers. Imex has set industry standards with its long-term warranties and educational support. *For more information on this revolutionary obstetrical Doppler, contact your nearest Imex representatives or call 1-800-525-2519.*



BIR Calendar

Unless otherwise indicated, enquiries should be addressed to the Conference Manager, British Institute of Radiology, 36 Portland Place, London W1N 4AT (Tel. 071-436 7807).

The Radiosensitivity of Human Tumours and Normal Tissues — How close to clinical application?
February 11, 1992
Organizer: Dr M. Saunders

Quality standards in nuclear medicine
February 18, 1992
Organizer: Dr A. Smith

3-D image analysis in medical imaging
February 25, 1992
Organizer: Professor M. A. Smith

Megavoltage portal imaging
April 10, 1992
Joint meeting with IPSM
Organizer: Dr W. Jones

Radiology & Oncology '92
18–20 May 1992
International Convention Centre, Birmingham

Computed Radiology - the opportunities
11 June 1992
Scientific Societies Lecture Theatre
Organizers: Mr A Budge, Mrs E Beckman

Measurement Techniques for Ultrasound Exposure
July 1, 1992
Organizer: Dr F. Duck

Conference Services

Is there a seminar, conference or evening get-together you want to organize, but you don't have the time? The BIR Conference Office may be able to help you. Please call Miss Vanessa Whitehead, Conference Manager, to discuss possibilities. Tel: 071-436 7807

Meetings and Courses

Magnetic Resonance Imaging
March 2-6, 1992
San Diego, California
Further details: Dawne Ryals, Ryals and Associates, P.O. Box 1925, Roswell, Georgia 30077-1925. Tel: (404) 641-9773. Fax: (404) 552-9859.

Head and Neck MRI at the University of L'Aquila
March 2-6, 1992
L'Aquila, Italy
Further details: Prof. R. Passariello, Radiology, Ospedale SM Collemaggio, 1067100, L'Aquila I, Italy. Fax: 39-682410997.

Skeletal Radiology Group of the Royal College of Radiologists
March 5-6, 1992
Coventry
Further details: Dr J Chandy, Consultant Radiologist, X-ray Department, Coventry & Warwickshire Hospital, Stoney Stanton Road, Coventry. Tel: 0203 224055.

Principles and Practice of Clinical MRI
March 5-8, 1992
Florida, USA
Further details: Programme Coordinator, Johns Hopkins Medical Institutions, Office of Continuing Education, Turner Building, 720 Rutland Avenue, Baltimore, Maryland 21205. Tel: 1 (301) 955-2959.

PET and SPECT Imaging of Living Brain Chemistry in Health and Disease
March 11-13, 1992
Maryland, USA
Further details: Program Coordinator, Johns Hopkins Medical Institutions, Office of Continuing Education, Turner Building, 720 Rutland Avenue, Baltimore, Maryland 21205, USA. Tel: 1 (301) 955-2959.

Study Day on Management of Pancreatic Cancer
March 24, 1992
University of Southampton
Further details: Mrs J Daniels, University Surgical Unit, F Level Centre Block, Southampton General Hospital, Tremona Road, Southampton, SO9 4XY. Tel: 0703 796144. Fax: 0703 794020.

International Symposium on Recent Advances in Diagnostic Imaging and Radiation Oncology
March 24-27, 1992
Kathmandu, Nepal
Further details: Dr Naresh Prasad, Dept. of Radiology, Baylor College of Medicine, Houston, Texas 77030, USA. Tel: (713) 798 4415. Fax: (713) 798 5556.

The Cambridge meeting on Chest Disease
March 25-27, 1992
Cambridge
Further details: Dr C D R Flower,\ Department of Diagnostic Radiology, Addenbrooke's Hospital, Hills Road, Cambridge CB2 2QQ. Tel: 0223 216203.

24th International Diagnostic Course in Davos - ABDOMEN
March 28-April 3, 1992
Davos, Switzerland
Further details: IDKD, PO Box 224, CH-8028, Zurich, Switzerland. Tel: 01 262-2404.

The Biological and Epidemiological Bias for Radiation Protection Standards
April 1-2, 1992
Oxford
Further details: Dr D N S Dixon, Programme Committee Secretary, The Society for Radiological Protection, 67 Oatlands Park, Linlithgow, West Lothian EH49 6AS. Tel: 031-244 2779.

6th Symposium Mammographicum
April 1-3, 1992
London
Further details: The Conference Office, The Royal College of Radiologists, 38 Portland Place, London, W1N 3DG. Tel: 071-636 4430. Fax: 071-323 3100.

Royal London Hospital/St. Bartholomew's FRCR Part 1 revision course
April 2-3, 1992
London
Further details: Dr P. Butler, Department of Neuroradiology, The Royal London Hospital, Whitechapel, London E1 1BB.

Institute of Biology National Conference: Biology in Europe after 1992
April 2-3, 1992
Southampton
Further details: Andrea Silvester or Nicola Beaney, Institute of Biology, 20 Queensberry Place, Loindon SW7 2DZ. Tel: 071-581 8333.

Eurodop '92: Major International Symposium on the Medical Applications of the Doppler Effect in Diagnostic Ultrasound
April 5-8, 1992
Brighton
Further details: Eurodop '92, Bell Howe Conferences, 1 Willoughby Street, Beeston, Nottingham NG9 2LT. Tel: 0602 436323.

Two-day workshop on Electronic Portal Imaging.
April 3-4, 1992
California, USA.
Further details: Dr Norman A Baily, Department of Radiology 0632, University of California, San Diego, 9500 Gilman Drive, La Jolla, CA 92093-0632. USA.

Resident's Radiology Review Course
April 19-24, 1992
San Diego, California
Further details: Dawne Ryals, Ryals and Associates, P.O. Box 1925, Roswell, Georgia 30077-1925. Tel: (404) 641-9773. **Fax:(404) 552-9859.**

Fleischner Society 22nd Annual Symposium on Chest Disease
May 7-8, 1992
Montreal, Canada
Further details: Fleischner Society, Meeting Management, 5665 Oberlin Drive, Suite 110, San Diego, CA 92121. Tel: (619) 453-6222. Fax: (619) 535-3880.

European Society of Gatro Intestinal Radiologists 3rd Annual Congress
22,23-24 June, 1992
Nice, France
Further details: Professor J M Bigot, Radiologist des Hopitaux, Hopital TENON 4, rue de la Chine, 75970, Paris.

Annual Meeting and Post-Graduate Course of the Cardiovascular and Interventional Radiological Society of Europe
August 30-September 3, 1992
Barcelona, Spain
Further details: CIRSE, P.O. Box 201, CH-8028 Zurich. Tel: (01) 262 24 04. Fax: (01) 261 05 78.

The 3rd AFSUMB '92: The 3rd Congress of Asian Federation of Societies for Ultrasound in Medicine and Biology
August 30-September 3, 1992
Seoul, Korea
Further details: Dr. Byung Ihn Choi, Department of Diagnostic Radiology, Seoul National University Hospital, 28 Yongon-Dong, Chongno-Gu, Seoul 110-744, Korea Tel: (822) 766-0930. Fax: (822) 766-0950

As a service to our readers, notices of meetings or courses will be inserted free of charge.
Please send articles for the Bulletin or any comments or suggestions you may have about the Bulletin to The Honorary Editor, BIR Bulletin, 36 Portland Place, London W1N 4AT.

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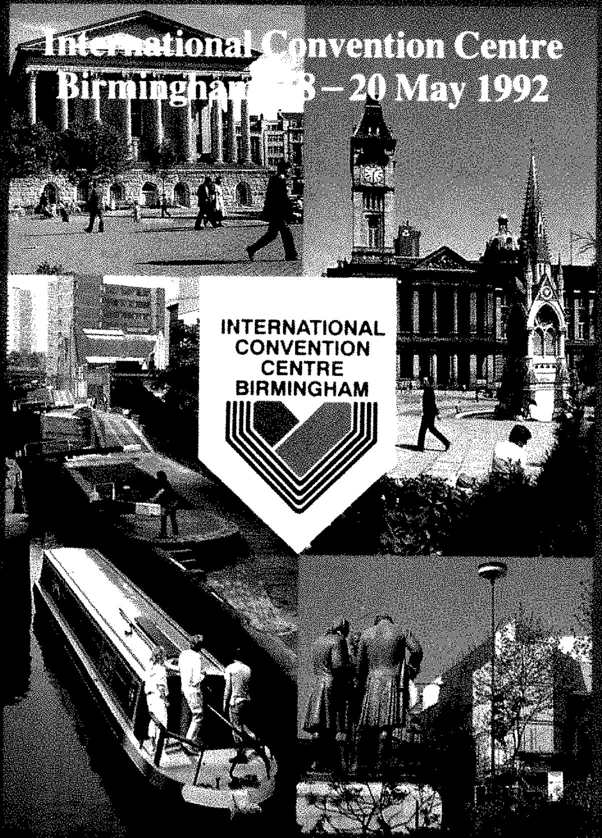
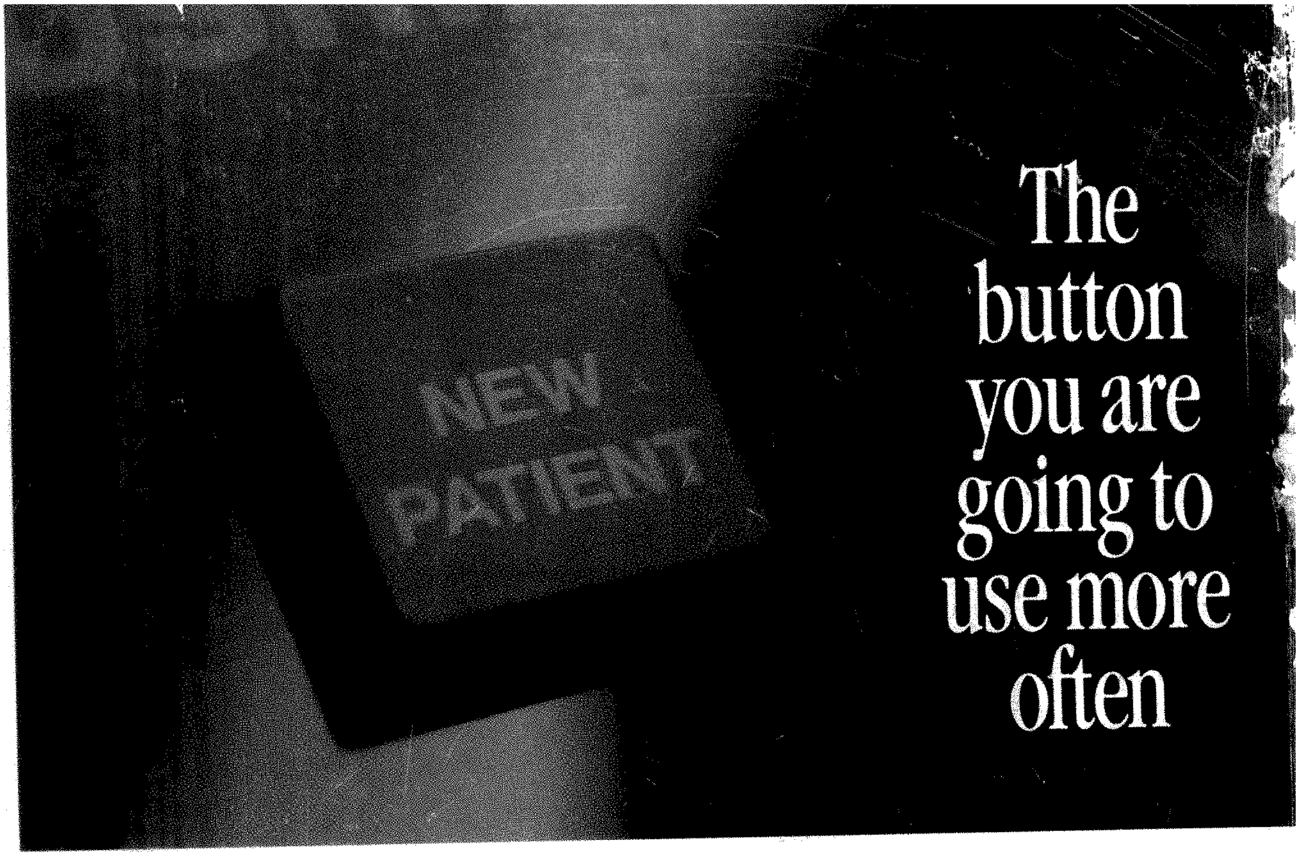
THE 50TH ANNUAL CONGRESS OF THE BRITISH INSTITUTE OF RADIOLOGY


International Convention Centre
Birmingham 18 – 20 May 1992



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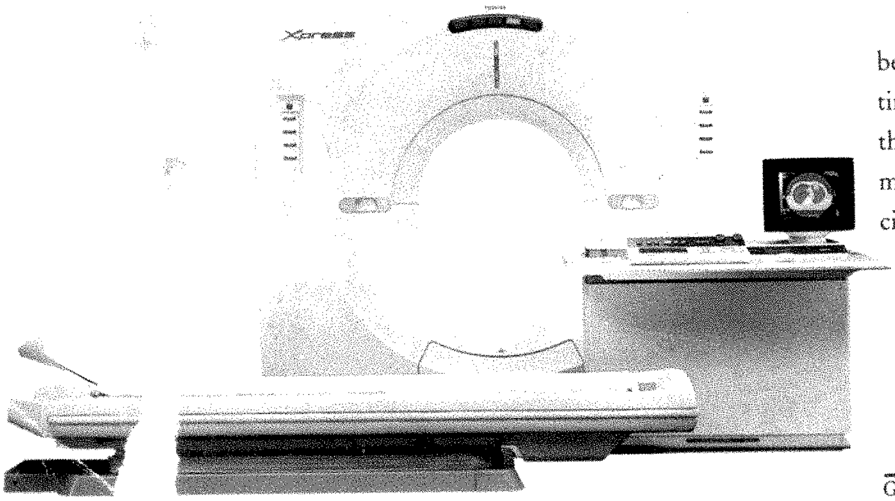

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